

Original Research Article

Study on haematological abnormalities in various stages of chronic kidney disease: stage 3-5

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ABSTRACT

Background: Chronic kidney disease is one of the major health problems worldwide and a major cause of morbidity and mortality. CKD is diagnosed on the basis of the presence of markers of kidney damage and kidney function. Aim of the study to assess the prevalence of hematological abnormalities in CKD (stage 3-5) and to assess their correlation among various etiologies of CKD (diabetes, chronic glomerulonephritis, hypertension).

Methods: The study was done in 150 cases diagnosed as CKD in the Department of Nephrology, IMCU, and in the medical ward at Tirunelveli Medical College Hospital. The diagnosis was based on an estimated GFR level $<60\text{ml/mt/1.73M}^2$. Total count, differential count, Hb, MCV, MCH, MCHC, WBC count, platelet count, and peripheral smear examination, coagulation profile were done on all the patients and results were compared and correlated with each other.

Results: In 150 patients, 90 males and 60 females were included. Among 90 males 43 were in stage 3 CKD, 11 in stage 4, 36 in stage 5. Among 60 females 7 were in stage 3, 39 in stage four, 14 were in stage 5. 63 patients had both hypertension and diabetes, 30 patients had only diabetes. There was a decrease in RBC, Total count platelet value with respect to increase in stages of CKD. There was a prolongation in BT, CT, PT, APTT and INR value in respect to increase in stages of CKD.

Conclusions: Chronic kidney disease patients have lower haematological indices and the degree of changes depends on the severity of kidney disease.

Keywords: Anemia, Coagulation, Chronic kidney disease, Haematology

INTRODUCTION

Chronic kidney disease has been a major public health problem. The hallmark of CKD is structural and/or functional damage to the glomeruli of the kidney. The most important result of renal damage is the loss of renal function and cardiovascular disease leading to premature death. CKD is a progressive condition and with the progress of the disease, the outcomes also progress to ultimately end up with kidney failure. Earlier stages of CKD can be detected through laboratory testing.

Accumulating evidence in the past 3 decades indicates that the identification of CKD in earlier stages can prevent its progression and delay the onset and progression of its outcomes. There have been discrepancies worldwide regarding the definition, classification and laboratory testing of CKD resulting in a lack of uniformity. In 2012, the National Kidney Foundation (NKF) and the Dialysis Outcomes Quality Initiative (DOQI) advisory board has approved the clinical practice guidelines to define the chronic kidney disease and stage CKD.¹ The workgroup developed the

following operational definition for chronic kidney disease (1) renal damage for ≥ 3 months as defined by structural or functional abnormalities of the kidney, with or without decreased glomerular filtration rate (GFR), manifest by either pathological abnormalities or markers of kidney damage, or abnormalities in imaging tests. (2) GFR less than 60ml/min/1.73m^2 for ≥ 3 months with or without kidney damage. CKD is not a static condition. It tends to progress and worsen overtime to ultimately end up with kidney failure because of the progress of the disease. There are certain risk factors that alter the initiation and progress of CKD and its outcomes in an adverse manner. CKD is also associated with certain complications the most important of which are anemia, hypertension, neuropathy and nutritional imbalance. Anemia is a common co-morbid finding in kidney failure patients. The patients with anemia in chronic kidney disease most frequently present with complaints pertaining to compromised renal functions. A patient with chronic kidney disease is said to be suffering from anemia if the hemoglobin concentration is $<13\text{g/dl}$ in adult males and if the Hb is $<12\text{g/dl}$ in adult females.²

This level of Hb is reached when the GFR is reduced to $<30\%$ of the normal value which corresponds to the serum creatinine level of $2\text{-}4\text{mg/dl}$. Irrespective of the type of CKD anemia can develop. Only in two conditions viz. polycystic kidney disease and hypertension usually anemia does not develop.³ The different morphological types of anemia occur in CKD. The normocytic normochromic type is the most common followed by the normocytic hypochromic type and microcytic hypochromic type which is the least common. While anemia being a most common finding in CKD patients, leucopenia and thrombocytopenia worsen as CKD stage progresses. This is probably because of inhibition of erythropoiesis, granulopoiesis and megakaryopoiesis, by the uremic inhibitors. Morphology of white blood cells appears within normal limits but clinically the patients present with an increased incidence of infections in uremia due to abnormal chemotactic function and defective receptor regulation.⁴ Also, a qualitative platelet defect occurs. There is decreased platelet adhesiveness and aggregation in response to adenosine diphosphate and decreased release of platelet factor III, due to the accumulation of toxic metabolites in uremia.⁵ The present study is an attempt at a comprehensive review of red blood cells (RBCs), leukocytes, platelets and coagulation profiles and to assess their significance in CKD.

Authors aimed to study the prevalence of hematological abnormalities in various stages of chronic kidney diseases (stage 3-5) and their correlation among various etiologies of CKD (DM/chronic glomerulonephritis/hypertension).

METHODS

Patients admitted as inpatients in the Department of Nephrology and medicine at Tirunelveli Medical College Hospital, during the period of August 2012 - October

2013 were included in this study of the prevalence of hematological abnormalities in various stages of CKD.

Inclusion criteria

- Patients with CKD (Stage 3-5)
- Age > 14 years

Exclusion criteria

- Paediatric patients
- Pregnant patients
- Patients with known hematological disorder
- H/O blood transfusion during the last 3 months
- Patients with ESRD treated with renal replacement in the form of dialysis and renal transplantation.
- Patients on drugs causing bone marrow suppression.

The details regarding age, sex, weight, monthly income the primary disease leading to CKD, tests used in diagnoses- ultrasound abdomen, blood urea, creatinine, urine- albumin sugar and were collected from the case charts. 50 patients in each stage of CKD.³⁻⁵ The number and percentage of each variable with respect to 50 patients were estimated. RBC count, hemoglobin and peripheral smear, total count, differential count, platelet count, PT, APTT, INR were compared and correlated with each other.

RESULTS

One hundred and fifty patients of CKD with an $\text{egfr} < 60\text{ml/mt}$ were included to study the prevalence of anemia and other hematological parameters. There were 90 males and 60 females in this study. Male predominance was observed. Among 90 males 43 were in stage 3 CKD, 11 in stage 4, 36 in stage 5. Among 60 females 7 were in stage 3, 39 in stage four, 14 were in stage 5. Male predominance in stage 3 and 5 CKD. In stage 4 CKD female was predominant. Maximum prevalence was observed in 51-65 yr age –group in stages 3 and 4. stage 5 CKD was prevalent in the 36-50 age group (Figure 1).

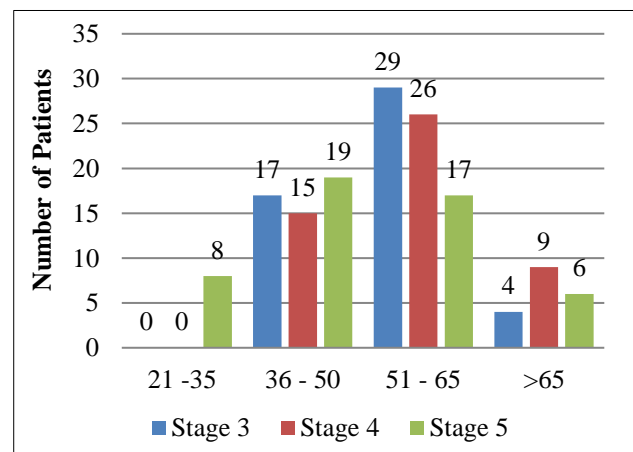


Figure 1: Age distribution and CKD stage.

Diabetes was the leading cause of CKD in this study followed by hypertension, 63 patients had both hypertension and diabetes, 30 patients had only diabetes. so total in 93 patients had diabetes was the underlying etiology (Figure 2).

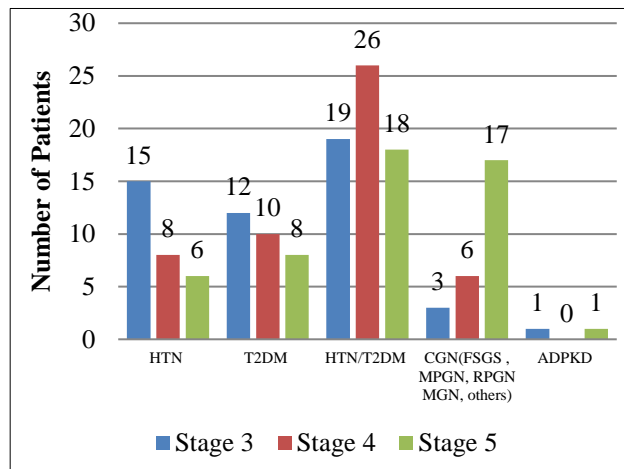


Figure 2: Classification CKD on etiology.

Among 90 males 61 patients had anemia. 26 were mildly anemic, 21 had moderate anemia, 14 were severely anemic. Among 60 females about 50 were anemic, 24 had mild anemia, 14 had moderate anemia, 12 had severe anemia (Table 1).

Table 1: Distribution of Hb in CKD patients.

Gender	Hb (gm/dl)	Stage 3	Stage 4	Stage 5
Male	<13	16	9	36
	>13	26	2	0
Female	<12	6	30	14
	>12	1	9	0

Table 2: Distribution of Hematology count.

Haematology	Stage 3	Stage 4	Stage 5	p value
RBC	3.26	2.83	1.38	<0.001
Total count	7678.4	6941.6	4557.2	<0.001
Platelet count	256460	207938	98640	<0.001
BT	2.44	3.24	5.1	<0.001
CT	4.04	4.6	6.58	<0.001
PT	12.96	13.31	16.03	<0.001
APTT	24.56	25.21	30.35	<0.001
INR	1.36	1.34	1.59	<0.001

In patients where CKD was due to diabetes, 12 male, and 12 female had anemia, 6 (4 male, 2 female) was not anemic. In patients with both diabetes and hypertension, 10 males and 18 females had anemia, 26 (20 male and 6 female) were not anemic. In patients with chronic glomerulonephritis, 11 males and 12 females had anemia. only 2 males and one female were not anemic. Anemia is highly prevalent in individuals, where diabetes and

chronic glomerulonephritis was the underlying etiology for CKD. In hypertensive nephrosclerosis, the percentage of females with anemia was more (Table 2).

NNA-normocytic normochromic anemia, MHA-microcytic hypochromic anemia, NHA-normocytic hypochromic anemia. In this study, there was a preponderance of normocytic normochromic anemia of 36%. A normal blood picture was seen in 33%. the microcytic hypochromic picture was seen in 12%. next common picture was normocytic hypochromic which was 10%. Pancytopenia was seen in 5% of individuals. Only 1% of individuals showed a dimorphic blood picture. Burr cells were present in 20 patients irrespective of peripheral smear picture and CKD stage.

In this study, RBC count progressively decreased as the stage declined. This fall was statistically significant with a p-value <0.001. The mean value of TC decreases stage by stage. The decreases are statistically significant ('p' value is < 0.001) This fall in platelet count as CKD stage declined was statistically significant. Bleeding time prolonged as CKD progressed. The mean value increased stage by stage. The increase was statistically significant (p value<0.001). In this study clotting time slightly prolonged as CKD progressed. The increase was statistically significant (p value-<0.001). In this study, it was found that prothrombin time tends to prolong as CKD stage declines in stage 3 CKD mean was 12.96. In stage 4 CKD, the mean was 13.31. In stage 5 CKD, the mean was 16.03. The prolongation of PT was statistically significant. In this study, APTT prolongs as CKD stage declines, 46 individuals in stage 3 and 4 CKD had normal APTT. Only four patients had prolonged APTT. But in stage 5 CKD thirty-six patients had prolonged APTT. Mean APTT in stage 3 was 24.56. In this study, INR tends to prolong as CKD stage declined mean INR in stage 3 was 1.362. Mean INR in stage 4 was 1.34. mean INR in stage 5 was 1.596 (Table 2).

DISCUSSION

Chronic kidney disease has been a major public health problem and a major cause of morbidity and mortality worldwide. The actual prevalence of the initial stages of CKD is much more than the later stages.

Coresh J et al have reported a prevalence of 3.3%, 3.0%, 4.3%, 0.2% and 0.2% respectively in stages 1, 2, 3, 4, 5 of CKD.⁶ However, in clinical practice prevalence of stages, 4 and 5 appears to be more because initial stages are asymptomatic and people present themselves when the severity of symptoms increases. Coresh J et al, and Viswanathan et al, have indicated that the prevalence of CKD is higher in older age groups with a male preponderance. The former has also reported that 11% of individuals older than 65 years have CKD.^{6,7}

The present study also showed predominance in older age, the maximum number of cases in stage 3 and 4 were

in the age group 51-65years. Cases in stage 5 were maximum in the 36-50 age group. The older age and the male predominance can be explained by the underlying disease entity causing CKD. Diabetes and hypertension, both of which are etiological factors of CKD are prevalent more in older age groups and male sex.⁶

CKD is a progressive condition and its progression is influenced by the underlying kidney disease leading to CKD and the presence of risk factors.² Among the etiology of CKD, as per the DOQI advisory board guidelines, diabetes is the most common cause followed by hypertension, vascular diseases, glomerular diseases, cystic diseases, and tubulointerstitial diseases.⁸

Hb levels decreased, indicating that the severity of anemia increased parallelly with the increase in the severity of CKD. The study done by Callen IR et al, showed that anemia becomes more severe as CKD progresses.⁹ This is because, as CKD progresses, inhibition of bone marrow, deficiency of EPO, deficiency of iron and bleeding tendencies increase as a result of an increase in the circulating uremic toxins.

Normocytic normochromic blood picture was the most common in the study with 36%, followed by microcytic hypochromic which was 12%. Then normocytic hypochromic picture which was 10%. This is also the scenario reported in the study by Callen IR et al, and in the study by the DOQI advisory board.^{9,10}

Certain morphological and quantitative alterations were noted with leukocytes, 40 patients showed leucopenia with a total count of less than 4000/cumm. In this study total count decreased as CKD stage declined. EPO is known to stimulate erythropoiesis with little effect on granulopoiesis. It is also possible that leukocytosis is a response to infection. It is possible that infections are due to impaired leukocyte function though they are increased in number. In our study platelet count declined as progressed. EPO deficiency is a possibility as EPO is known to stimulate megakaryocytopoiesis to some extent. In this study bleeding time and clotting time prolonged as CKD stage declined, indicating uremia is prone to abnormalities in hemostasis. Also, prothrombin time, APTT, INR tends to prolong as the CKD stage declined.

CONCLUSION

CKD is prevalent in the adult population with a male predominance in older age 51-65 groups. Diabetes and hypertension are the commonest etiological factors of CKD. Anemia is a common complication of CKD and the degree of anemia increases as CKD worsens. Mild anemia with normocytic normochromic pictures with sparse distribution of RBCs is the most common picture. Etiological correlation - anemia and other hematological abnormalities were prevalent, irrespective of the underlying etiology causing the

CKD. Leucopenia was observed, which worsened as CKD progressed. Thrombocytopenia is observed which worsened as CKD progressed. Both bleeding and thrombotic tendencies were observed as CKD worsened. Chronic kidney disease patients have lower haematological indices and the degree of changes depends on the severity of chronic kidney disease.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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