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Study of Hematological Profile in Chronic Renal Failure Patients on Hemodialysis in a Tertiary Care Hospital

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ABSTRACT

Background: Chronic Kidney Disease is a cause of high morbidity and mortality in developing nations like India. The various hematological parameters and their correlation to different stages of CKD help assess the severity, prognosis and outcome of these patients.
Methods: A hospital based cross-sectional observational study was done to detect the prevalence of haematological abnormalities, correlation of anaemia, typing of anemia with CKD stages(stages 3 to 5) of the patients were included in this study. Presence of anaemia (Hb%, MCV, peripheral smear), RDW, thrombocytopenia, leucocyte count, differential count in different stages of CKD were studied.
Result: The 96.8%subjects in the study group are anemic with normocytic and normochromic findings on peripheral smear. 57.3% patients had High TLC but no significant association was established with High TLC with increasing stage of CKD. MCV and Platelets were within normal limits with only slight variation. Increased RDW has a positive correlation with CKD.
Conclusion: The CKD patients have various changes in the blood parameters especially anemia and iron studies should be carried out so that treatment for that should be started and improve the quality of life in CKD patients.

Keywords: *Anaemia in CKD, Chronic kidney disease, Haematological abnormalities in CKD, Iron deficiency anaemia, Thrombocytopenia.*

INTRODUCTION

Chronic Kidney Disease (CKD) is one of the major health problems worldwide. The morbidity and mortality related to Chronic Kidney Disease is always of great concern in developing nation like India. It is estimated to affect 10% of the general population and affects 50% of the high risk population [(1)] which comprises of elderly who already suffer from spectrum of non communicable diseases like type-2 Diabetes Mellitus and Hypertension [(2)].

According to KIDGO 2012 guidelines, CKD is defined as abnormalities of kidney structure or function, present for 3 months, with implications for health.

CKD is classified based on cause, GFR category, and albuminuria category (CGA). On the basis of GFR, CKD have been categorized into stages (total of 5 stages) and according to that treatment of the patient is started. [(3)] CKD encompasses a wide range of physiological processes altered by the progressive decline in glomerular filtration rate (GFR).[(4,5)] Haematological parameters have shown various changes particularly red blood cell (RBC) indices, are most commonly affected,[(6)] giving rise to anemia.

MATERIALS AND METHODS

The objective of this study is to obtain the hematological abnormalities like

Anemia, Thrombocytopenia and leukocytosis in patients undergoing hemodialysis. The correlation of these abnormalities with Stage of CKD is also carried out.

A total of 128 cases are studied and all the patients which are taken in the study are ESRD for at least past 3 months seeking hemodialysis in our hospital. All age groups are taken into account. Patients' creatinine and Urea levels are obtained. Through patients Creatinine and other details, eGFR is calculated and they are categorized into CKD stages. Stage1 with GFR of >90ml/min/1.73m^2 and Stage 5 with GFR of <15 ml/min/1.73m^2.

The CBC sample of the patient is run on 6- part Sysmex XN -1000 hematology analyser. The hematological parameters which are taken in our study are Hemoglobin levels, Total count, Differential count, platelet count, Red cell Distribution width (RDW) and Mean Corpuscular Volume (MCV). The peripheral smear examination of the CBC samples is done ON slides are stained with Fields and Leishman stains and observed under the microscope.

RESULTS

128 cases on hemodialysis are divided according to the stage of CKD. 95 (74.4%) cases were in stage 5, 28 (21.7%) cases were in stage 4 and 5 (3.9%) cases in stage 3.

Age and Sex

The cases studied ranged from age group of 9 to 86 years.

CKD was more common in males, out of 128 cases, 92 (71.8%) were males and 36 (28.2%) were females. Hence, Male Gender was more prone to CKD.

Anemia

Anemia is most common complications of CKD. According to KIDGO 2012 guidelines, diagnosis of anemia in adults and children under 15 years with CKD when the Hb concentration is 13.0 g/dl (130 g/l) in males and 12.0 g/dl (120 g/l) in females.

In the present study, 96.8% patients had anemia. Severity of anemia was correlated with the stages of CKD. Hemoglobin of 7gm% was considered severe, 7-11 gm % was considered moderate and more than 11gm% was mild anemia. (Table-1)

Table-1 Distribution of Hemoglobin

Hb(gm%)	*CKD stage 3*	*CKD stage 4*	*CKD stage5*
< 7	2 (40%)	16 (57.14%)	59 (62.11%)
7-11	2 (40%)	11 (39.29%)	32 (33.68%)
>11/<13	0	0	1 (1.05%)
>13	1 (20%)	1 (3.57%)	3 (3.16%)

The study presented with 62.1% of Stage-5 CKD patients with severe anemia and 57.1% of stage 4 CKD patients with only 3.16% of Stage 3.

3.57% of Stage 4 patients had Hemoglobin more than 11gm%. The mean value of Hb in CKD patients was 7.49. Mean Hb was highest in stage 3 indicating there is positive relationship of degree of anemia with stage of CKD. The probability value or the p value for presence of anemia in CKD patient has come around <0.5% indicating positive correlation.

Stage 5 CKD patients had statistically significant anemia with Hemoglobin levels less than 9gm% ($p<0.05$) (Table-2)

Table-2 –Mean and Standard of deviation of Hemoglobin

Stage	Mean(Hb-gm%)	Standard of Deviation
III	8.98	3.62
IV	7.27	2.05
V	7.48	6.05

Peripheral Smear Examination

The peripheral examination was done for all the patients and Anemia typing was done of the patients with Hb less than 13.

Normocytic Normochromic Anemia was present in (113) 91.1% of the patients of which 76% cases were Stage -5 CKD. Microcytic Anemia was present in 5.6% of the patients. Macrocytic and Dimorphic was present in only 1.56% cases each. (Table-3)

Table-3: RBC morphology in Anemias - Stagewise

Morphology	*Stage-3*	*Stage-4*	*Stage-5*	*Total*
Normocytic Normochromic	***4***	***23***	***85***	***113***
Microcytic Hypochromic	***0***	***1***	***6***	***7***
Macrocytic	***0***	***1***	***1***	***2***
Dimorphic	***0***	***2***	***0***	***2***

Total Leucocyte count

Of the 129 patients, 74 (57.3%) patients showed normal Total leucocyte count, 35(27.1%) patients showed Leucocytosis and 20 (15.5%) patients showed Leucopenia. Patients with High TLC were majority of Stage-5 CKD patients and had Polymorphonuclear Leucocytosis in almost (95.9%) all of them except for 3 cases. (table-4)

Table-4: Stage wise Total Leucocyte Distribution.

WBC count	Stage-3	Stage-4	Stage-5	Total
Leucocytosis	3	7	25	35
Normal Count	2	19	53	74
Leucocpenia	0	2	18	20
Total	5	28	96	12
Mean	17522	11104	9803	10389
Standard Deviation	***9941.2***	***7985.61***	***7437.68***	***7745.15***

Mean Corpuscular Volume

The mean Of the MCV for the CKD patients is 87.50. The P value of MCV with stage of CKD was >0.05 contemplating as Not Significant. (Table-5)

Table-5: Stage wise MCV Distribution.

MCV	Stage-3	Stage-4	Stage-5
<83	0	4 (14.29%)	23(24.11%)
83-100	4(80%)	23(82.14%)	67(70.53%)
>100	1(20%)	1(3.57%)	6(5.26%)
Mean	92.44	86.84	87.43
Std Deviation	9.86	9.45	9.79

Platelets

The mean platelet of the 128 CKD patient came out to be 1.87 Lakhs/cumm which is in normal range of the normal platelet count (1.5-4.5 Lakhs/cumm). (Table-6)

Table-6: Stage wise Mean Platelet Distribution.

Platelet	Stage-3	Stage-4	Stage-5
Mean	1.74	2.20	1.78
Std Dev	0.60	2.06	1.06

Red Cell Distribution Width

The mean RDW for all the 128 cases was 16.37 which is more than the normal RDW. 60% of the stage 5 cases showed RDW more than >15. The p Value for the presence of CKD and increased RDW is <0.05 and thus Significant. (Table-7)

Table-7: Stage wise RDW Distribution.

RDW	Stage-3	Stage-4	Stage-5
<15	80%	78.5%	60%
>=15	20%	21.5%	40%
Mean	16.22	17.33	16.09
Std.Dev	2.04	4.72	2.02

DISCUSSION

In this hospital based study we have taken into account the hematological parameters of the CKD patients with Low GFR (<60ml/min/m2).

Majority of CKD patients were male which was similar to studies done by Pandurang et al [7], Chakravarti et al [8] and Arun et al [9].

The mean age of the patients With CKD was

In this study, 96.8% patients had anemia which is in concordance with Chinwuba et al [10], Islam et al [11] and Bhattacharjee et al[12]. Only 5 patients had hemoglobin > 13 gm% out of 128. The hemoglobin distribution was categorized into mild, moderate and severe and then prevalence of anemia in different stages of CKD was obtained. It showed Stage 5 CKD to have statistically significant anemia for Hb<9gm% which was similar to studies by Chakravarti et al[8] and Dewan et al[13]. The major cause of anemia in CKD patients is lack of Erythropoetin (EPO) synthesis in the the damaged or injured peritubular cells in kidneys resulting in low levels of EPO and thus anemia. As the anemia is because of low EPO levels it is of usually of Normocytic and Normochromic Types. But as with the CKD, there is decline in the nutritional status of the patients due to repeated Dialysis and inadequate intake which may give Microcytic Hypochromic or Macrocytic or Dimorphic anemias. The 2012 Kidney Disease Improving Global Outcomes (KDIGO) guidelines recommended that CKD-5 D patients should maintain Hb concentrations ≥10 g/dL. In patients with Hb <10 g/dL, therapy should

be individualized based upon the rate of fall in Hb concentration, the response to iron therapy, risk of transfusion, the risks related to ESA (Erythropoetic stimulating agent) therapy, and the presence of symptoms. In CKD-5 Dialysis patients, KDIGO suggests initiating therapy when the Hb concentration is <10 g/dL.[3]

An adequate Hb target for anemia improves physiologic and clinical parameters and quality of life. [22-24] Adequate iron stores are essential to optimize the effects of ESA, such as recombinant human erythropoietin (EPO) or darbepoetin alfa. In fact, decreased iron stores or decreased availability of iron represent the most common cause for resistance to the effect of these agents. The two best test of iron status are the serum ferritin and the present transferrin saturation (TSAT).[25] The distinction between absolute and functional iron deficiency is essential to understanding what constitutes adequate TSAT & circulating ferritin concentrations in ESA-treated CKD patients. In normal subjects, iron deficiency is considered "absolute" when iron store is depleted (circulating ferritin levels <12 ng/mL, and iron delivery is impaired as indicated by TSAT below 16%). Absolute iron deficiency in CKD patients has been defined as a circulating ferritin values <100 ng/mL and TSAT levels lower than 20%. Differently, functional iron deficiency results when there is a need for a greater amount of iron to support hemoglobin synthesis than can be released from iron stores. This clinical situation can be observed in a chronic pharmacological stimulation with ESA in CKD patients with adequate iron stores, and it is characterized by a reduction in TSAT percent despite normal or elevated circulating levels of ferritin [26,27].

The typing of anemia on the peripheral smear showed predominantly to be Normocytic Normochromic (91.1%) in morphology which was in concordance with many studies such as of Chakravarti A et al [8], Mudiyammanarava NR et al [14], Dewan P et al [13], Reza et al [16], Arun S et al [9] and George SV et al [15]. Tennakore KK et al [18] have proved association of macrocytosis with increased mortality in hemodialysis CKD patients.

The mean WBC count for the patients was within normal range.57.3% of patients showed normal WBC count. 27.1% showed Neutrophilic Leucocytosis of which majority of cases (71.3%)where in Stage-5 which was similar to the studies done by George et al [15], Chakravarti et al [8] and Rathod SG et al [17]. Only 1.56% cases had macrocytic anemia.

Redden et al [20] have concluded by their study that patients with neutrophilic leukocytosis were associated with increased mortality risk. Septic shock is the most common cause of death in patients of hemodialysis and various studies have proved it so early recognition and aggressive fluid therapy and early antibiotics administration can prevent sepsis and eventually mortality in these patients.[21]

The Mean Corpuscular Volume (MCV) is long being used diagnostic approach of anemia in clinical practise. The mean MCV was 87.3 and it was within the normal range. 5.25% of Stage 5 Patients showed MCV >100.

Various studies have proved correlation of high MCV with increased mortality in CKD patients [19]. The underlying mechanism is not fully known. The only possible explanation for this is MCV is also the biomarker of malnutrition. A higher MCV may also points towards bone marrow dysfunction with altered hematopoiesis. The term megaloblastic anemia without macrocytosis indicates the presence of folate or vitamin B12 deficiency without apparent macrocytosis. Therefore, these findings could also be explained by the above phenomenon in that, the MCV is increased with no evidence of Macrocytosis on peripheral smear.[19]

The Mean platelet count was in the reference range. In our study 43.7% cases showed platelet count less than 1.5 lakhs / cumm with 25% cases showed platelets less

than 1 lakhs/ cumm with only 3.25% cases with platelets less than 0.5 lakhs/cumm. The study done by Gaffer et al [28] showed decrease in platelet count and mild thrombocytopenia in CKD patients which was similar to Dorgaleh et al [29] and Kaw et al[30].The decrease in platelets counts can be because of two reasons first it can decreased production and increased destruction. The cause of low platelets in hemodialysis patients can be because of increased destruction of platelets which might be drug induced as in many clinical settings the anticoagulant drug used for hemodialysis is Heparin which is known to produce immune response resulting in production of antibodies which causes destruction of platelets [31]. Di Mino G et al [32] suggested that the platelet function in chronic renal failure patients is also jeopardized. Under normal conditions, ADP and serotonin are secreted to attract more platelets. In renal failure patients, their platelet granules have decreased levels of ADP and serotonin. Platelets count and Function are both decreased in CKD patients. Further workup is required to come to conclusion.

The mean RDW in our study was on higher side and was statistically was on the higher side. Red cell distribution width (RDW) is a quantitative marker of the variability in size of erythrocytes. Elevated RDW reflects increased size variations of red blood cells which indicate altered erythrocyte life span or dysfunctional erythrocytes. Various authors hypothesized that the size variations of erythrocytes reflected the functional iron status and functions of bone marrow .[33-34] Studies done by Hyung Jung Oh and Molnar et al showed High RDW as independently and closely associated with mortality in any sort renal impairment patients or heart disease patients. The study done by Hikmet Tekce et al [35] reflected negative effects of inflammation, malnutrition, and interdialytic excess weight gain on RDW elevation in an HD study cohort with sufficient iron storage and without anemia and hypervolemia. Furthermore, endothelial dysfunction, microalbuminuria, which is a marker of cardiovascular risk, inflammation, and increased oxidative stress have been suggested as responsible of increased mortality. However, these mechanisms are still controversial. [35] Prospective multicentric studies should be carried out to assess the underlying pathophysiology of the High RDW in CKD patients.

CONCLUSION

In our study we find that anemia was prevalent 96.8% cases and the cause of anemia is understood to low erythropoietin levels but the data of that is not available in this study. Hb less than 9 gm% was statistically significant in CKD patients. Normocytic normochromic morphology was seen in majority of anemias. Neutrophilic Leucocytosis was seen in 27.3% cases and suggests underlying infective etiology in these patients. Platelet count was on the lower side in 43.7% cases and thus further platelet function and coagulation studies should be carried out to know the underlying cause. MCV was within the normal limits. RDW was raised and statistically significant suggesting further workup to know the underlying pathophysiology.

With this study you come to know how the various hematological parameters varies in hemodialysis patients and how these parameters can affect the prognosis and further management in these patients.

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