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Original Research Article

Hematological changes in patients of chronic renal failure and the effect of hemodialysis on these parameters

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ABSTRACT

Background: Chronic kidney disease (CRD) is a global public health problem, where slowly progressive deterioration in kidney function lead to numerous hematological and biochemical dysfunction which further make the patients vulnerable to cardiovascular morbidity and mortality if appropriate measures is not taken for their control. The aim of present study was to find out the common hematological dysfunction that may occur in the patients of chronic renal failure (CRF) and in the process of dialysis and suggest appropriate measures for their management.
Methods: Forty-two patient with CRF and on regular maintenance dialysis and 40 healthy adults were recruited into the study. Hemoglobin concentration, total red cell count, total white blood cell count and platelet count and ESR were assessed for the subjects and controls. Results were analyzed using SPSS 21.0 version.
Results: showed that the RBC count, hemoglobin levels and platelets counts are significantly reduced in the patients of chronic renal failure and the process of hemodialysis further decreases the level of all the above mentioned hematological parameters whereas there is slight increase in total leucocyte count but significant increase in ESR was detected.
Conclusions: Chronic renal failure is associated with different degrees of abnormality in hematological parameters that needs careful evaluation and management.

Keywords: Chronic renal failure, Hematological parameters, Hemodialysis

INTRODUCTION

Chronic kidney disease (CKD) is a global public health problem, with greater burden and very high cost of care especially in developing countries like India. The National Kidney Foundation in India states that, kidney diseases rank 3rd amongst the life-threatening diseases after cancer and heart disease. About 200,000 persons landed into terminal kidney failure every year and millions more suffer from lesser forms of kidney diseases.[1] End-Stage Renal Disease (ESRD) is the final stage of CRF characterized by progressive, irreversible deterioration in renal function and body fails to maintain fluid and electrolyte balance resulting in uremia. ESRD is characterized by a decrease in GFR and evidence of less than 10% nephron function remaining.[2] During hemodialysis (HD) essential kidney functions, such as the elimination of water and metabolic wastes as well as the correction of the electrolyte and acid/base state, are replaced by the artificial purification system. Elements such as Na+, K+, Ca++, Mg+, Cl-, and H+ must be kept in a rather narrow physiological range, otherwise life-threatening events may occur.[3] Kidney diseases are associated with a change in various biochemical and hematological parameters. Anemia parallels the degree of renal impairment and the most important cause is failure of renal erythropoietin secretion. Other factors include chronic blood loss, hemolysis and bone marrow

suppression by retained uremic factors.[4-6] The most affected ones are erythrocyte indices. This is because majority of erythropoietin is synthesized in the juxta glomerular apparatus except 10% in liver and other organs. Apart from decreased erythropoietin, changes in red blood cells (RBCs) indices may be caused by vitamin B12, iron and folic acid deficiencies, which are consequences of dietary insufficiency or blood loss or by decreased erythrocytes' life span.[7,8] Other causes of anemia in CKD may include gastrointestinal bleeding; severe hyperparathyroidism and systemic inflammation.[9] Other affected hematological parameters in CKD include total leukocytes and its differential counts, platelet count, bleeding time and prothrombin time. White blood cells (WBCs) count, platelet count and bleeding time were within normal ranges in CKD subjects.[10] Other findings reported include eosinophilia and prolonged bleeding time.[11] Thrombocytopenia is regarded as a consequence of hemodialysis. However, its occurrence is rare in patients undergoing hemodialysis using biocompatible membranes.[12] Platelet count tends to be decreased in both predialysis and hemodialysis patients.[13] Moreover, renal impairment, anemia and other clinical complications in hemodialysis patients may be commonly related to increased cellular uptake and toxicity of aluminum. Trace elements play an important role in the structure of proteins, enzymes and complex carbohydrates to participate in biochemical reactions. It also involved in a number of metabolic activities, including nerve conduction, transport excretory processes and serving as cofactors for enzymes. The cells of the proximal renal tubule have an important role in the homeostasis of essential metals, and the kidney is a target site for metal toxicity.[14] Biochemical and hematological profiles are commonly affected in CKD and this becomes more apparent as the disease progresses which further complicates the condition of the patient, making the patient more vulnerable for cardiovascular complications. Few literatures exist on hematological profiles of subjects with CKD in our environment. The objective of this study is to assess the hematological profile of our subjects with CKD and the effect of dialysis on these parameters.

METHODS

This is a cross sectional study on the patients of chronic kidney disease and on maintenance hemodialysis. The study was carried out in the HAHC hospital which is attached to Hamdard institute of medical sciences and research, Jamia Hamdard, New Delhi between January-2017 to july-2017.

The study population are the patients attending dialysis unit of HAHC hospital. The selection of patients was based on previous diagnosis with chronic kidney disease, based on KDIGO guidelines (CKD is defined as either kidney damage marked by albuminuria and GFR less than 60 mL/min per 1.73 m^2 for ≤3 months).[15] Source of data was patient's dialysis unit records and personal interview with the patient and / or his relative with follow ups. A pre-tested structured questionnaire was used to elicit the information regarding the socio-demographic characteristic disease and drug history and lab investigations.

Blood samples

Blood samples were taken with anticoagulant for haematological investigations such as RBC, haemoglobin, TLC, DLC, ERS and Platelet etc.

Inclusion criteria

All the patients suffering from chronic kidney disease and ware > 15 years of age.

Exclusion criteria

- Patients suffering from any disease other than CKD that could affect their haematological parameters such as malignancy, inherited or acquired blood diseases, acute or chronic inflammation, connective tissues diseases, dehydration, or recent hemorrhagic episode were excluded from the study,
- Pregnant and lactating women.

RESULTS

Out of total 42 patients undergoing hemodialysis and enrolled for the study, 40 were followed and completed the study (one patient died during the study period due cardiovascular complications and one left the study due to change of residence). Among the study population 30 (75%) patients were male and 10 (25%) were female, the maximum number of patients were from the age group 41-60 years (60%) followed by the patients of age group 21-40 years (20%) (Table 1).

Table 1: Age and gender distribution of hemodialysis patients.

Age (year)	Male	Female	Total no.
< 20	00	02	02
21 - 40	06	02	08
41- 60	20	04	24
>60	04	02	06
Total	30	10	40

Primary cause of ESRD leading to dialysis: The most common primary etiology for ESRD leading to dialysis was patient suffering from both diabetes and hypertension 35% followed by hypertension alone 25% and diabetes mellitus 20% (Table 2).

Chronic comorbidity in dialysis patients: Among the presence of co-morbidity, hypertension with diabetes mellitus topped the list (40%) followed by hypertension (25%), diabetes mellitus (15%) and coronary artery disease (5%) (Table 3).

Table 2: Primary cause of ESRD leading to dialysis.

Primary cause	Number of patient	% of patient
Hypertension	10	25
Diabetes mellitus	08	20
Diabetes mellitus with hypertension	14	35
Drug intake	04	10
Kidney stone	03	7.5
Chronic glomerulonephritis	01	2.5

Table 3: Chronic comorbidity in dialysis patients.

Co-morbid conditions	Number of patients	% of patients
Hypertension only	10	25
Diabetes mellitus	06	15
Hypertension with diabetes Mellitus	16	40
Cardiovascular disease	02	05

Effect of chronic kidney disease on hematological parameters and its relationship with hemodialysis: data presented in Table 4 shows that the RBC count, hemoglobin levels and platelets counts are significantly reduced (p-value < 0.05) in the patients of chronic renal failure and the process of hemodialysis further decreases the level of all the above mentioned hematological parameters whereas there is slight increase in total leucocyte count in the patient of CRF but a significant leukocytosis is induced by the process of dialysis (Table 4).

Table 4: Hematological parameters in hemodialysis patients and its relationship with hemodialysis.

Parameters (mean values)	Control (mean value)	Pre-dialysis (mean value)	Post-dialysis (mean value)
Hb (gm/%)	12.6	8.84	7.6
RBC (million/mm3)	4.8	3.76	3.06
TLC(thousand/mm3)	5.7	6.06	6.76
Platelet count (lac/mm3)	2.62	1.73	1.57
ESR	14.8	52.5	42.16

Another significant change noted was in the value of ESR which is significantly high (p-value <0.05) in the patients of chronic renal failure and dialysis also has significant role in decreasing ESR value in these patients.

Effect of chronic kidney disease on differential leucocyte count and its relationship with hemodialysis: although there is some leukocytosis in the patients of chronic renal failure there is not much effect of CRF on DLC except that an increase in number monocyte was detected (Table 5).

Table 5: Differential leucocyte count in patients of CRF and its relationship with hemodialysis.

Differential leucocyte count (mean value)	Control (%) (mean value)	Pre-dialysis (%) (mean value)	Post-dialysis (%) (mean value)
Neutrophil	62	64.22	67.5
Lymphocytes	22	20.3	19.15
Monocyte	04	10.45	9.8
Eosinophil	2.5	0.8	0.8
Basophil	0.1	0.47	0.22

DISCUSSION

It has been observed in our study that the Hb concentration and RBCs count are decreased in chronic renal failure patients when compared with control. This finding is in agreement with study obtained by other authors.[16] The essential cause of decrease RBC counts and consequent decrease in the Hb concentration and packed cell volume in chronic renal failure is impaired erythropoietin production and other factors which suppress marrow erythropoiesis and shortened red cell survival. RBC survival is decreased in uremic patients in proportion to the blood urea nitrogen concentration, and it improves significantly after intensive hemodialysis. Uremic plasma increases the expression of phosphatidyl serine on the outer cell surface in red blood cells. This enhances the recognition of damaged red blood cells by macrophage, leading to their subsequent destruction and decreased survival.[17] Anemia is the most common, consistent and severe form of the various hematological abnormalities.[18] Although anemia may be found at different CKD stages, a strong correlation exists between the incidence of anemia and the degree of CKD severity.[19] In addition to anemia, patients with chronic renal failure are prone to develop infections and hemorrhagic diathesis.[20] In the present study the platelet count was decreased among chronic renal failure patients. Erythropoietin potentiates the effect of megakaryocyte colony stimulating factors, acetlyhydroase (PAF-AH) and paraoxonase (PON1). In chronic renal disease, impaired

erythropoietin secretion leads to a decrease in platelet count.[21] The detection of receptors for erythropoietin in megakaryocytes is understandable, because erythropoietin levels can affect platelet level and because of extensive homology between erythropoietin and thrombopoietin, erythropoietin act as the major humoral regulator of platelet mass.

Abnormal haemostasis in chronic renal failure is characterized by tendency to abnormal bleeding and bruising. Decreased factor III activity, abnormal platelet aggregation and adhesiveness and impaired prothrombin consumption contribute to the clotting defect in uremia.[22] Although hemostatic defects in uremia are often complex, it is probable that platelet dysfunction is the most consistent and clinically the most important feature.[23] Macrocytosis in chronic hemodialysis patients may be associated with increased mortality.[24] CRF is associated with many kinds of metabolic changes caused by the kidney disease and also attributable to dialysis treatment. Phenomena such as accumulation or deficit of various substances and dysregulation of metabolic pathways combine in the pathogenesis of these changes.[25]

In the process of accumulation, decreased urinary excretion plays a crucial role and leads to retention of metabolites in the body (e.g., creatinine, urea, electrolytes, and water). The increased formation of metabolites through catabolic processes and alternative metabolic pathways also wields an influence. Regular dialysis treatment partly decreases this accumulation but cannot avert the overall deficit. This deficit of some important substances in CRF can be caused by deficient intake in diet, impaired intestinal absorption, or increased losses during dialysis sessions. Disturbed synthesis of some crucial metabolic regulators (e.g., erythropoietin, active vitamin D) in kidneys also plays an important role. All of the above-mentioned factors lead to many serious complications for CKD patients during the course of dialysis and dialysis. All accelerate development of atherosclerosis, malnutrition-inflammation complex syndrome (MICS), anemia, hyperparathyroidism, and other serious problems that markedly affect prognosis and the quality of life of patients with CKF.[26,27]

It is well known that hematological parameters are reduced in CKD. The most affected ones are erythrocyte indices. This is because majority of erythropoietin is synthesized in the juxta glomerular apparatus except 10% in liver and other organs. Apart from decreased erythropoietin, changes in red blood cells (RBCs) indices may be caused by vitamin B12, iron and folic acid deficiencies, which are consequences of dietary insufficiency or blood loss or by decreased erythrocytes' life span.[28,29] Other causes of anemia in CKD may include gastrointestinal bleeding; severe hyperparathyroidism and systemic inflammation.[30]

The use of recombinant human erythropoietin in hemodialyzed has replaced transfusions and led to major improvement of the survival rates of CKD-associated anemic patients.[31] Other affected hematological parameters in CKD include total leukocytes and its differential counts. White blood cells (WBCs) count, in our study was slightly raised in CRF patients and also process of dialysis further increases WBC count this may be due to up regulation and presence of cytokines such as tumor necrosis factor –α (TNF-α) and interleukin-6 (IL-6) in blood contribute to chronic inflammation in the uremic state, the inflammatory response is characterized by an obvious presence of pro-inflammatory cytokines.[32] This presence implies activation of the acute phase proteins such as C - reactive protein which may also be the cause of significantly raised ESR value found in our study and decreased level of these chronic inflammatory mediators during the process of hemodialysis also decreases the ESR value.[33]

Thrombocytopenia is regarded as a consequence of hemodialysis. Platelet count tends to be decreased in both predialysis and hemodialysis patients.[34] However, its occurrence is rare in patients undergoing hemodialysis using biocompatible membranes.[35] Many studies found a statistically significant decrease in platelet count of CKD patients.[36-38]

CONCLUSION

Chronic renal failure is associated with different degrees of abnormality in hematological parameters that needs careful evaluation and management.

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REFERENCES

1. National Kidney Foundation: K/DOQI Clinical Practice Guidelines for Anemia of Chronic Kidney Disease. Am J Kidney Dis. 2006;47 (Suppl 3): S33-S53.
2. Poothullil J, Shimizu A, Day RP, Dolovich J. Anaphylaxis from the product (s) of ethylene oxide gas. Ann Intern Med. 1975;82(1):58-60.
3. Daugirdas JT, Ing TS, Roxe DM, Ivanovich PT, Krumlovsky F, Popli S, et al. Severe anaphylactoid reactions to cuprammonium cellulose hemodialyzers. Archives of internal medicine. 1985;145(3):489-94.
4. Levin A, Bakris GL, Molitch M, Smulders M, Tian J, Williams LA, Andress DL. Prevalence of abnormal serum vitamin D, PTH, calcium, and phosphorus in patients with chronic kidney disease: results of the study to evaluate early kidney disease. Kidney international. 2007;71(1):31-8.
5. Hsu CY, Bates DW, Kuperman GJ, Curhan GC. Relationship between hematocrit and renal function

in men and women. Kidney international. 2001;59(2):725-31.
6. Locatelli, F. Pozzoni P and Del Vecchio L, Recombinant Human Epoietin beta in the Treatment of Renal Anaemia. Ther Clin Risk Manag. 2007; 3(3): 433-9.
7. Locatelli F, Pozzoni P, Del Vecchio L. Recombinant human epoetin beta in the treatment of renal anemia. Therapeutics and clinical risk management. 2007;3(3):433.
8. Eschbach JW Jr, Funk D, Adamson J, Kuhn I, Scribner BH and Finch CA. Erythropoesis in patients with renal failure undergoing chronic dialysis. N. Eng J. Med.1967;276(12): 653-8.
9. Ratcliffe PJ. Molecular biology of erythropoietin. Kidney international. 1993;44(4):887-904.
10. Akinsola A, Durosinmi MO, Akinola NO. The haematological profile of Nigerians with chronic renal failure. Africa J Medic and medical Sci. 2000;29(1):13-6.
11. Oluboyede OA, Williams AIO (1995). Serum ferritin and other Iron Indices in Adult Nigerians with Chronic Renal Failure: Review of Management of Anaemia. Afr J. Med. Med. Sci.; 24:231-237.
12. Katz I. Kidney and kidney related chronic diseases in South Africa and chronic disease intervention program experiences. Advances in chronic kidney disease. 2005 Jan 31;12(1):14-21.
13. Gafter U, Bessler H, Malachi T, Zevin D, Djaldetti M, Levi J. Platelet count and thrombopoietic activity in patients with chronic renal failure. Nephron. 1987;45(3):207-10.
14. Boosalis MG. The role of selenium in chronic disease. Nutrition in Clinical Practice. 2008;23(2):152-60.
15. National kidney foundation. K/DOQI Clinical Practical Guidelines for Chronic Kidney Disease, Evaluation, Classification and stratification. Am J. Kidney Dis. 2002; 39 (Suppl 1): 51-5266.
16. Suresh M, Mallikarjuna RN, Sharan B, Singh M, Hari Krishna B, Shravya KG. Hematological changes in chronic renal failure. Int J Sci Res Publ. 2012;2(9):1-4.
17. Means RT, Glader B. Acquired nonimmune hemolytic disorders. Wintrobe's Clinical Hematology. 2009;1:1021-37.
18. Brown GE, Roth GM; The anemia of chronic nephritis. Arch Intern Med.1922; 30(6): 817-840.
19. McClellan W, Aronoff SL, Bolton WK, Hood S, Lorber DL, Tang KL, et al. The prevalence of anemia in patients with chronic kidney disease. Current medical research and opinion. 2004;20(9):1501-10.
20. Castaldi PA, Rozenberg MC, Stewart JH; The bleeding disorder of uraemia. 1966; 2(7454): 66-69.
21. Ch. Gouva, E. Papavasiliou, K.P. Katopodis, A.P. Tambaki, D. Christidis and A.D. Tselepis. Effect of Erythropoietin on Serum paf-acetylhydrolase in patients with Chronic Renal Failure. Nephrology dialysis transplantation. 2006: 21(5):1270-77
22. Cheney K, Bonnin JA. Haemorrhage, platelet dysfunction and other coagulation defects in uraemia. Brit J Haematol. 1962;8(3):215-22.
23. Marcus AJ; Platelet function. New Engl J Med. 1969; 280(24): 1330-1335.
24. Tennankore KK, Soroka SD, West KA, Kiberd BA. Macrocytosis may be associated with mortality in chronic hemodialysis patients: a prospective study. BMC nephrology. 2011;12(1):19.
25. Cibulka R, Racek J, Vesela E. The importance of L-carnitine in patients with chronic renal failure treated with hemodialysis. Vnitrni Lekarstvi. 2005;51(10):1108.
26. Durak I, Akyol Ö, Başeşme E, Canbolat O, Kavutcu M. Reduced erythrocyte defense mechanisms against free radical toxicity in patients with chronic renal failure. Nephron. 1994;66(1):76-80.
27. Silver J, Kilav R, Sela-Brown A, Naveh-Many T. Molecular mechanisms of secondary hyperparathyroidism. Pediatric Nephrology. 2000;14(7):626-8.
28. Locatelli F, Pozzoni P, Del Vecchio L. Recombinant human epoetin beta in the treatment of renal anemia. Therapeutics and clinical risk management. 2007;3(3):433.
29. Eschbach Jr JW, Funk D, Adamson J, Kuhn I, Scribner BH, Finch CA. Erythropoiesis in patients with renal failure undergoing chronic dialysis. New England Journal of Medicine. 1967;276(12):653-8.
30. Ratcliffe PJ. Molecular biology of erythropoietin. Kidney international. 1993;44(4):887-904.
31. Fink JC, Blahut SA, Reddy M, Light PD. Use of erythropoietin before the initiation of dialysis and its impact on mortality. Americ J Kidney Dis. 2001;37(2):348-55.
32. Tbahriti HF, Meknassi D, Moussaoui R, Messaoudi A, Zemour L, Kaddous A, Bouchenak M, et al. Inflammatory status in chronic renal failure: The role of homocysteinemia and pro-inflammatory cytokines. World J Nephrol. 2013;2(2):31.
33. Castillo-Rodríguez E, Pizarro-Sánchez S, Sanz AB, Ramos AM, Sanchez-Niño MD, Martin-Cleary C, et al. Inflammatory Cytokines as Uremic Toxins:"Ni Son Todos Los Que Estan, Ni Estan Todos Los Que Son". Toxins. 2017;9(4):114.
34. Gafter U, Bessler H, Malachi T, Zevin D, Djaldetti M, Levi J. Platelet count and thrombopoietic activity in patients with chronic renal failure. Nephron. 1987;45(3):207-10.
35. Katz I. Kidney and kidney related chronic diseases in South Africa and chronic disease intervention program experiences. Advances in chronic kidney disease. 2005;12(1):14-21.
36. Suresh M, Mallikarjuna RN, Sharan B, Singh M, Hari Krishna B, Shravya KG. Hematological changes in chronic renal failure. Int J Sci Res Publ. 2012;2(9):1-4.
37. Yassein RB., Alseedig NO, Abd Allah SK, Mohmmed AA, Alballah NA, Syid MA. (2016). Hematological parameters among Sudanese patients

with chronic renal failure. Internat J Res Granthaalayah. 2016;4(16):50-4.
38. Alghythan AK, Alsaeed AH. Hematological changes before and after hemodialysis. Scientific Research and Essays. 2013;7(4):490-7.

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