

Hematological Changes in Chronic Renal Failure

Suresh M^{*}, Mallikarjuna reddy N^{**}, Sharan B Singh M^{**}, Hari Krishna Bandi^{***}, Shravya keerthi G^{**},
Chandrasekhar M^{*}

^{*} Dept of Physiology, Meenakshi Medical College and Research institute (MMCH and RI), Kanchipuram, India.

^{**} Dept of Physiology, Narayana Medical College (NMC), Nellore, Andhra Pradesh, India.

^{***} Dept of Physiology, Jawaharlal institute of postgraduate medical education and research (JIPMER), Puducherry

Abstract- Background: Kidney diseases is ranked – 3rd amongst life threatening disease in India, after cancer and heart disease. About 200,000 persons go into terminal kidney failure every year. Erythropoietin is the primary regulator of red blood cell formation in the bone marrow, which are mostly produced by the renal epithelial cells. This study was carried out to observe the hematological changes like RBC count, Hb concentration, hematocrit, platelet count and TLC in patients suffering from chronic renal failure.

Materials and Methods: 50 Chronic renal failure patients blood samples were compared with 50 age and sex matched controls with inclusion criteria of age between 30 to 75 years, serum creatinine > 1.5 mg/dl, and exclusion criteria of serum creatinine < 1.5 mg/dl and patients suffering from muscular atrophy. Haematological parameters were estimated by using Beckman coulter automatic analyzer, and the serum creatinine was estimated by fully automated random access chemistry analyzer.

Results: Data were analyzed statistically by T – test and Pearson's correlation coefficient test. In chronic renal failure patients, RBC count HB concentration, hematocrit and platelet count were significantly (P<0.05) reduced, whereas TLC was reduced but not statistically significant.

Conclusion: Chronic renal failure patients have lower hematological indices, due to impaired production of erythropoietin, and other factors like increase haemolysis, suppression of bone marrow erythropoiesis, hematuria and gastrointestinal blood loss. The concentration of serum creatinine shows negative correlation with all the haematological parameters. And the degree of changes depends on the severity of renal failure.

Index Terms- Erythropoietin, hematocrit, platelet count and creatinine.

I. INTRODUCTION

Normal renal function is very important for homeostasis, so much so, that situations in which renal functions are impaired can be life threatening. Diseases of the kidneys are among the most important causes of death and disability in many countries 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 200,000 persons go in to terminal kidney failure every year. Million more suffer from lesser forms of kidney diseases. [2]

In United States 35,000 deaths are attributed yearly to renal diseases. The rate of kidney disease mortality in the United States has increased by 52% in the past 16 years and continues to be higher in blacks than whites.[3] Morbidity however is by no means insignificant. Millions of persons are affected annually by non fatal kidney diseases, most notably infections of the kidney or lower urinary tract, kidney stones and urinary obstruction. Twenty percent of all women suffer from infection of the urinary tract of kidney at sometime in their lives and at least 1% of the U.S. population develops renal stones. [4]

Chronic Renal Failure (CRF)

Chronic renal failure is a syndrome characterized by progressive and irreversible deterioration of renal function due to slow destruction of renal parenchyma, eventually terminating in death when sufficient numbers of nephrons have been damaged. Acidosis is the major problem in CRF with development of biochemical azotemia and clinical uraemia syndrome. [4]

Renal diseases are associated with a variety of haemopoietic changes. Anemia parallels the degree of renal impairment and its most important cause is failure of renal erythropoietin secretion. Other factors include chronic blood loss, hemolysis and bone marrow suppression by retained uremic factors. [5]

The aim of the present study is to find out the hematological changes in chronic renal failure patients.

II. MATERIALS AND METHODS

Effects of Chronic renal failure on Hematological parameters is a cross -sectional study, in which hematological tests were conducted in 50 Chronic renal failure patients and compared with 50 age and sex matched controls. The subjects were selected under the age between 30to 75 years and serum creatinine >1.5 mg/dl, and exclusion criteria of serum creatinine < 1.5 mg/dl and patients suffering from muscular atrophy.

Hematological parameters like Red Blood Cell count (RBC), Haemoglobin concentration (Hb %), Packed cell volume (PCV), Platelet count and Total Leucocyte count (TLC) were estimated by using Beckman coulter automatic analyzer, and the serum creatinine was estimated by fully automated random access chemistry analyzer (Humastar 300).

III. RESULTS

The RBC count, Hemoglobin concentration, Hematocrit & Platelet count is decreased in chronic renal failure patients, which is statistically significant (P= 0.0001). Total leukocyte count is

decreased in chronic renal failure patients, which is not statistically significant (P= 0.380). The serum creatinine level is increased in chronic renal failure patients, which is statistically significant (P= 0.0001). Serum creatinine shows negative

correlation with all the hematological parameters. Serum creatinine is increased and is statistically significant.

Table-1

Name of the group	RBC (million/mm ³)	Hb gm%	PCV %	Platelet (Lakhs/mm ³)	TLC (Thousands/mm ³)	Creatinine (mg/dl)
Control group(n=50)	4.83±0.36	13.49±0.88	40.92±2.41	2.88±0.55	8376±1507	0.95±0.22
Study group(n=50)	3.06±0.65	8.83±1.78	27.13±4.41	1.59±0.57	8054±2156	4.76±2.29
P- Value	0.0001	0.0001	0.0001	0.0001	0.38	0.0001

IV. DISCUSSION

The hematological parameters in 50 chronic renal failure patients compared with 50 age and sex matched controls. In our study, it has been observed that the RBC count is decreased (Table-1) in chronic renal failures. (P<0.0001, highly significant). Primary cause of decrease RBC count in chronic renal failure is impaired erythropoietin production and other factors which suppress marrow erythropoiesis and shortened red cell survival. Erythropoietin is the hormone which is the major humoral regulator of red cell production and helps to maintain the viability of RBC by retarding the cleavage of DNA that occurs normally in CFU-Es. In the absence of EPO, DNA cleavage is rapid and leads to cell death.

RBC survival is decreased in uremic patient's in proportion to the blood urea nitrogen concentration and, it improves significantly after intensive hemodialysis. Uremic plasma increases the expression of phosphatidylserine 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. [6]

The hemolytic factor implicated in decreased red blood cells survival is presumed to be a toxic substance normally excreted or metabolized by the kidneys, one such substance is guanidine and its derivatives which appear to be a subset of the many retained metabolites, adversely affect erythrocyte survival. [7]

The hemoglobin concentration and hematocrit are decreased (Table-1) in chronic renal failure patients. (P < 0.0001, highly significant). The hemoglobin concentration and hematocrit generally provide an accurate reflection of the extent to which

the circulating red cell mass is reduced. In chronic renal disease because of impaired erythropoietin secretion, increased destruction of red blood cells, leads to a fall in red blood cell count, which reduces the hemoglobin concentration and hematocrit. A decrease in hematocrit is apparent even among patients with mild to moderate renal insufficiency. [8]

An inverse relationship between serum or plasma erythropoietin levels with hemoglobin (Hb) concentration and hematocrit (PCV) normally exist. As the hemoglobin and hematocrit decreases the erythropoietin level rises. The known negative correlation between serum erythropoietin and Hb and PCV was not apparent in our study, probably because of loss of renal mass leading to decreased erythropoietin in spite of anemia's.

It has been observed that the platelet count is decreased (Table-1) in chronic renal failure patients. (P< 0.0001, significant). Erythropoietin potentiates the effect of megakaryocyte colony stimulating factors, acetylhydroase (PAF-AH) and paraoxonase (PON1). In chronic renal disease, impaired erythropoietin secretion leads to a decrease in platelet count(55). 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.

In patients with chronic renal disease treated with erythropoietin, a minor increase in platelet count, averaging approximately 30,000 per microliter has been noted. The decrease in platelet count in patients with chronic renal disease leads to prolonged bleeding time and altered haemostasis. [9]

It has been observed that the total leukocyte count (TLC) is reduced than the control, (Table-1) which is not statistically significant. ($P = 0.38$). The precise mechanism by which chronic renal disease leads to a slight decrease in total leukocyte count is not clear. The possible hypothesis is as follows.

In chronic renal failure patients undergoing dialysis, in the dialyser, exposure of blood to artificial membranes may result in complement activation in vivo. The complement is typically C3a or C5a, produced by the classic complement activation pathway. Complement activation induces neutrophil aggregation and adherence to endothelial surface with resultant fall in total leukocyte count. In patients undergoing hemodialysis the incidence of this affect may be as high as 20%.[10]

The serum creatinine level is increased in chronic renal failure patients. ($P < 0.0001$, highly significant). (Table-1) chronic renal disease, creatinine clearance is affected which results in increased serum creatinine. Estimation of serum creatinine is used as a diagnostic test to assess kidney function. Creatinine level more than 1.5 mg/dl indicates impairment of renal function. Serum creatinine shows negative correlation with all the haematological values. [11]

V. CONCLUSION

From the present study it can be concluded that Patients with chronic renal failure show abnormal haematological parameters. It has been proposed that in chronic renal failure, impaired production of erythropoietin is the main reason for the decrease in red blood cell count, hemoglobin concentration, hematocrit, platelet count and total leukocyte count. Other associated factors like increase haemolysis, suppression of bone marrow erythropoiesis, hematuria and gastrointestinal blood loss may play a role in decrease red blood cell count, haemoglobin% and hematocrit.

The concentration of serum creatinine shows negative correlation with all the haematological parameters. Chronic renal failure patients have lower haematological indices and the degree of changes depends on the severity of chronic renal failure.

REFERENCES

- [1] R.L.Bijlani. Applied renal physiology. In: Understanding medical physiology. Third edition. JP Brothers, New Delhi. 2004; 8.4: 522-23.
- [2] National Kidney Foundation: K/DOQI Clinical Practice Guidelines for Anemia of Chronic Kidney Disease. Am J Kidney Dis. 2006;47 (Suppl 3): S33-S53.
- [3] Yael Waknine. Kidney disease mortality rates continue to increase. Medscape Medical News, Morbidity and Mortality Weekly report. March 16, 2007.
- [4] Charles E. Alpers. The Kidney. In: Vinay Kumar, Abul K. Abbas and Nelson Fausto. Robbins "pathologic basis of disease", Seventh edition, Elsevier Inc: 2004; 20: 960-65.
- [5] Dodds A. Nicholls M. Haematological aspects of renal disease. Pub Med – index for medline. 1983; 11(4): 361-68.
- [6] Michael R. Jeng and Bertil Glader. Acquired nonimmune hemolytic disorders. In: John P. Greer, John forester, John N. Lukens, George M. Rodgers and Frixos Paraskevas. Wintrobe's clinical hematology. Eleventh edition, 2004; Vol – 1, chapter 38: 1239.
- [7] Robert T. Means Jr. Anemias secondary to chronic disease and systemic disorders. In: John P. Greer, John forester, John N. Lukens, George M. Rodgers, Frixos Paraskevas and Bertil Glader. Wintrobe's clinical hematology. Eleventh edition, 2004; Vol – 1, chapter 47: 1451-55.
- [8] Emmanuel N. Dessypris and Stephen T. Sawyer. Erythropoiesis. In: John P. Greer, John forester, John N. Lukens, George M. Rodgers, Frixos Paraskevas and Bertil Glader. Wintrobe's clinical hematology. Eleventh edition, 2004; Vol – 1, chapter 07: 208-12.
- [9] 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.
- [10] Raymond G.Walts. Neutropenia. In: John P. Greer, John forester, John N. Lukens, George M. Rodgers, Frixos Paraskevas and Bertil Glader. Wintrobe's clinical hematology. Eleventh edition, 2004; vol – 2, chapter 63: 1784.
- [11] Victor W. Rodwell. Conversion of amino acids to specialized products. In: Robert K Murray. Harper's Illustrated Biochemistry. Twenty sixth edition, McGraw hill: 2003: chapter 31: 267.
- [12] Akio Urabe, Fumimaro Takaku, Hideaki Mizoguchi ,et al. Effect of recombinant human erythropoietin on the anemia of chronic renal failure. The International Journal of Cell Cloning 1996; Volume 6 Issue 3:179 – 91.
- [13] Alans G.O., Jingrong Yang, Lynn M. Ackerson, Krista Lepper, and Sean Robbins, Barry M. Massie. Hemoglobin level, chronic kidney disease and the risks of death and Hospitalization in Adults with Chronic Renal Failure. Journal of American Heart Association 2006: 113: 2713 –23.
- [14] Arthur C.Guyton and John E.Hall. kidney diseases and diuretics. In:Text book of medical physiology. Tenth edition, Elsevier India Pvt Lit. chapter : 31, 406-09.
- [15] Chi – Yuan Hsu, Charles E. McCulloch and Gary C. Curhan. Iron status and hemoglobin level in Chronic Renal Insufficiency. J Am Soc Nephrol. 2002: 13: 2783 –86.
- [16] Chi-Yuan Hsu, David W Bates, Gilad J Kuperman and Gary C Curhan. Relationship between hematocrit and renal function in men and women. Kidney International. 2001: 59: 725–31.
- [17] David E Leaf and David S Gold Farb. Interpretation and review of health related quality of life data in CKD patients receiving treatment for anemia. Kidney International. 2009: 75: 15 – 24.
- [18] DM Vasudevan and Sreekumari. Clinical biochemistry – kidney function test. In: Textbook of Biochemistry. Third edition: 2001: chapter 53: 436 – 42.
- [19] Druke T, Locatelli F and Clyne N. Normalization of hemoglobin level in patients with chronic kidney disease and anemia. N Engl J Med. 2006: 355: 2071-84.
- [20] Elísio Costa, Susana Rocha, Petronila Rocha -Pereira, Elisabeth Castro, Flávio Reis and Frederico Teixeira. Altered Erythrocyte membrane band 3 profile in Chronic Renal Failure Patients under Haemodialysis. Actas Bioq. 2008: 9: 73-77.
- [21] G. Remuzzi, M. Livio, G. Marchiaro, G. Mecca and G. de Gaetano. Bleeding in Renal Failure: Altered Platelet Function in Chronic Uraemia only Partially Corrected by Haemodialysis. Nephron Jorunals 1978; 22: 347-53.
- [22] Hamid Nasri. Influence of Serum Homocysteine on platelet count in Stable Hemodialysis Patients. Pak J Physiol. 2006: 2(2).
- [23] Harsh Mohan. The kidney and lower urinary track. In:Text book of pathology, Fifth edition, Jeypee brothers (P) Ltd.2005 (20) – 677-78.
- [24] HW Radtke, A Claussner, PM Erbes, EH Scheuermann, W Schoeppe and KM Koch. Serum erythropoietin concentration in chronic renal failure: relationship to degree of anemia and excretory renal function. The American Society of Hematology. 1979: Volume 54, Issue 4, pp. 877 –84.
- [25] Iijima S, Otsuka F, Takita T and Kikuchi Y. Leukopenia and rheological anomalies in leukocytes during hemodialysis in patients with chronic renal failure. Nephron ISSN 0028-2766, 1996, vol.74,561-66.
- [26] Indu khurana. Red blood cells and anaemias. In Text book of medical physiology. Elsevier, 2006;3.2:149-50.
- [27] J. Metz. Observations on the Mechanism of the Haematological Changes in the Haemolytic Uraemic Syndrome of Infancy. British Journal of Haematology. 1972: 23 (Suppl.): 53.
- [28] Jean-Christophe Luthi, W Dana Flanders, Michel Burnier, Bernard Burnand and William M McClellan. Anemia and chronic kidney disease are associated with poor outcomes in heart failure patients. BMC Nephrology. 2006: 7: 3.

- [29] John B. West. The red blood cells. In: Best and Taylor's Physiological basis of medical practice. 12th edition, New Delhi: B.I. Waverly Pvt Ltd. 1996: chapter no 23: 369-375.
- [30] Jon J Synder, Robert N Foley and David T Gilbertson. Hemoglobin levels and Erythropoietin doses in Hemodialysis and Peritoneal Dialysis patients in the United States. *J Am Soc Nephrol.* 2004; 15: 174 –79.
- [31] K Twoo and Fracp. Am. Retarding the progression of Chronic Renal Failure. *Singapore J.* 1991: Vol 32: 299 – 300.
- [32] Khanam S, Begum N, Begum S and Hoque EAM. Changes in Hematological Indices in Different Stages of Chronic Renal Failure. *J Bangladesh Soc Physiol.* 2007 Dec; (2): 38-41.
- [33] *Kidney International*, Hemoglobin variability in epoetin-treated hemodialysis patients Vol. 64 (2003), pp. 1514–21.
- [34] Locatelli F, Contef and Marcelli D. The impact of Hematocrit levels and erythropoietin treatment on overall and cardiovascular mortality and morbidity – The experience of the Lombardy Dialysis. *Registry Nephrol Dial Transport.* 1998; 13: 1642 –44.
- [35] M. Livio, G. Remuzzi, G. Marchiaro, G. Mecca and G. de Gaetano. Bleeding in renal Failure: Is U on willebrand factor implicated. *British Medical Journal.* 1977: 2: 359 – 61.
- [36] Mark wormwood. Iron deficiency anaemia and iron over load. In: S. Mitchell LEWIS, Barbara J. Bain and Imelda bates. *Dacie and Lewis Practical Haematology.* tenth edition, 2006 Elsevier Ltd, chapter7:131 – 135.
- [37] Mittal and Kher V. Chronic Renal Failure in India. *Ren Fail.* 1997 Nov; 19 (6): 763 – 70.
- [38] Mo U. Gafter, H. Bessler, T. Malachi, D. Zevin, M. Djaldetti and J. Levi. Platelet Count and Thrombopoietic Activity in Patients with Chronic Renal Failure. *Nephron Journals.* 1987; 45: 207-210.
- [39] Mohamed Ali MS, Babiker MA, Merghani LB, Ali FA and Abdulmajeed MH. Hematological Changes Post-Hemo and Peritoneal Dialysis Among Renal Failure Patients in Sudan. *Saudi J Kidney Dis Transpl.* 2008; 19: 274-279.
- [40] N. Udayakumar. Chronic Kidney Disease in Developing Countries; A silent Epidemic. *Postgraduate Medical Journal.* 2006; 82: 697 – 698.
- [41] National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis.* 2002; 39(suppl 1): S1-S266.
- [42] NKF – DOQI. Clinical practice guidelines for the treatment of anemia of chronic renal failure. National Kidney Foundation. *Am J Kidney Dis.* 1997: (suppl 3): S192 – S240.
- [43] P C Sharpe, Z R Desai and T C M Morris. Increase in mean platelet volume in patients with chronic renal failure treated with erythropoietin. *J Clin Pathol.* 1994; 47: 159-161.
- [44] Schrier RW, Wang W, Poole B and Mitra A. Acute renal failure. *J.Clin Invest* 2004,114 (1) 5-14.
- [45] Singh A, Saczech L and Tang KL. Correction of anemia with epoetin alpha in chronic kidney disease. *N Engl J Med.* 2006: 355: 2085-2098.
- [46] T. R. Mitchell and G. D. Pegrum. Oxygen Affinity of Haemoglobin in Chronic Renal Failure. *British Journal of Haematology.* 2009: **Volume 21 Issue 4: Pages 463 – 72.**
- [47] Talwar VK, Gupta HL and Shashinarayan. Clinicohaematological profile in chronic renal failure, *J Assoc Physicians India.* 2002 Feb; 50:228-33.
- [48] Victoria S Lim, Jerry Fangman, Michael J Flanigan, Richard L Degowin and Robert T Abels. Effect of recombinant erythropoietin on renal functions in humans. *Lancet.* 2:1175 –78.
- [49] Victor W. Rodwell. Conversion of amino acids to specialized products. In: Robert K Murray. *Harper's Illustrated Biochemistry.* Twenty sixth edition, McGraw hill: 2003: chapter 31: 267.
- [50] William M. McClellan, W. Dana Flanders, Robert D. Langston, Claudine Jurkowitz, and Rodney Presley. Anemia and Renal Insufficiency Are Independent Risk Factors for Death among Patients with Congestive Heart Failure Admitted to Community Hospitals: *Am Soc Nephrol.* 2002; 13: 1928–1936.

AUTHORS

First Author: Suresh M, Dept. of Physiology, Meenakshi Medical College & Research Institute (MMCH&RI), Kanchipuram, India.

Second Author: Mallikarjuna Reddy N, Dept. of Physiology, Narayana Medical College (NMC), Nellore, India.

Third Author: Sharan B Singh M, Dept. of Physiology, Narayana Medical College (NMC), Nellore, India.

Fourth Author: Hari Krishna Bandi, Dept. of Physiology, Jawaharlal Institute of Post graduate Medical Education and Research (JIPMER), Puducherry India.

Fifth Author: Shravya Keerthi G, Dept. of Physiology, Narayana Medical College (NMC), Nellore, India.

Sixth Author: Chandrasekar M, Dept. of Physiology, Meenakshi Medical College & Research Institute (MMCH&RI), Kanchipuram, India.

Corresponding Author: Suresh M, Dept. of Physiology, Meenakshi Medical College & Research Institute (MMCH&RI), Kanchipuram, India. , Email: sureshsuha.bhuvan@gmail.com
Mobile: +918883019714