Hematological indices of end-stage chronic renal failure patients in Sudan: With or without iron supplements

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Abstract: Anemia is very common among end stage patients with chronic renal failure (CRF). In this investigation, hematological parameters were examined in patients with end stage chronic renal failure from Khartoum, Sudan. A total of 70 patients and additional 30 healthy subjects were included in the study. All patients were under erythropoietin therapy whereas 42% were using iron supplements. The results showed that about 98% of CRF patients had anemia. Normocytic normochromic anemia was the most common type (94%) while few were suffering from microcytic hypochromic (6%) anemia. Low levels of hemoglobin, red blood cell count, hematocrits, serum iron, serum ferritin, and platelet counts were observed in the patient group compared to healthy controls ($P<0.01$). However, MCV, MCH and MCHC were not different between the two groups ($P>0.05$). Moreover, no significant differences in all hematological parameters between patients with and without iron supplements were observed except for hemoglobin. In conclusion, anemia is common among end stage CRF in Sudan in spite of erythropoietin and iron therapy.

Keywords: Renal failure, kidney, blood, anemia, erythropoietin, iron supplements.

INTRODUCTION

The kidney is a vital organ that eliminates waste from the blood and ensures electrolyte balance in the body fluids (Torban and Goodyer, 2009, Xu, Nie *et al*., 2018). The functional units inside kidney are glomeruli, which are tiny bundles of capillaries (Gnudi, Benedetti *et al*., 2015). A decrease in the glomerular filtration rate below 60 mL/min/1.73 m^2 indicates a health condition known as chronic renal failure (CRF) or chronic kidney disease (Collister, Ferguson *et al*., 2016). The disease is characterized by the loss of kidney function over a period of time (Ye and Mao, 2016). Diabetes, hypertension, and polycystic kidney disease are among the reported caused of CRF (Collister, Ferguson *et al*., 2016, Ye and Mao, 2016). The symptoms of CRF include decreased urine secretion, presence of blood and proteins in urine, edema, fatigue, hypertension and others (Weisbord, 2007).

The global prevalence of all stages of CRF is estimated to be close to 13%, while patients in the end stages represent about 0.5% of the population (Hsu and Powe, 2017). This high prevalence suggests high burden to health systems (Stel, Bruck *et al*., 2017). CRF is associated with increased risk of cardiovascular diseases and premature death (Cosola, Rocchetti *et al*., 2018).

Previous studies have shown significant decreases in the production of red blood cells in patients with CRF, which is attributed mainly to erythropoietin deficiency (Dorgalaleh, Mahmudi *et al*., 2013). This leads to the development of anemia, which usually begins with the early stages of the disease and becomes more severe in the advanced stages (Zadrazil and Horak, 2015). In addition, several studies have also reported significant decreases in platelet count in CRF patients. Among the types of detected anemia is normocytic and normochromic red blood cell, which is the most common complication of CRF (Kutuby, Wang *et al*., 2015). In addition, microcytic and hypochromic are also present in some CRF patients (Ramanath, Gupta *et al*., 2012).

In the current study, we investigated the prevalence of anemia among CRF patients from Sudan. In addition, hematological parameters were compared in patients with or without iron supplements.

MATERIALS AND METHODS

Study participants

The study is case-control and descriptive in design that was conducted at the Kidney Transplantation Association Hospital, Khartoum, Sudan. A total of 70 patients with chronic renal failure were included in the study. For comparisons, 30 healthy subjects from the same geographical area were included to serve in the control group. Written informed consents were obtained from study participants according to the institutional review board of Sudan University of Science and Technology and Kidney Transplantation Association Hospital, Khartoum, Sudan.

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Blood sampling

Venous blood samples were collected from participants in both EDTA tubes and plain tubes. Blood samples were used directly for hematological evaluations.

Hematological parameters

Blood collected in EDTA tubes was used for complete blood count (CBC) analysis, which was performed using an automated hematological analyzer (XE-2100 -Sysmex analyzer). EDTA blood samples were also used to prepare thin blood films using Leishman stain for RBCs morphology. Blood collected in plain tubes was centrifuged to harvest serum. Serum iron and ferritin levels were measured using chemistry analyzer (Selectra ProXL Clinical Chemistry System).

STATISTICAL ANALYSIS

The Statistical Package for Social Science software program (SPSS version 21) was used for statistical analysis. Two group comparisons were conducted using Students-t test or Chi square test as appropriate. Sample size calculations were obtained using an online statistical software: http://powerandsamplesize.com/Calculators/. A p value <0.05 was set as a threshold for significant difference.

RESULTS

In this study, 70 patients with chronic renal failure from Kidney Transplantation Association Hospital in Khartoum, Sudan were included in the study. In addition, 30 healthy individuals were recruited to serve in the control group. The sample characteristics are shown in table 1. The mean age of the patient group was 46.8 years compared to 42.7 years in the controls. The gender ratio was similar between the two groups (1:1 in the controls compared to 1.3: 1 in the patients). All patients were under erythropoietin therapy (50-100 unit per kg per week) while 42% were taking iron supplements (ferrous sulphate, 300 mg tablet, three times daily). Finally, 98.5% of the patient group suffer from anemia compared to 0% in the control group. The types of anemia among patients group are shown in fig. 1. About 94% of patients suffer from normocytic normochromic anemia while 6% suffer from microcytic hypochromic.

Table 2 shows comparisons of hematological parameters between controls and patients. Significantly lower levels of hemoglobin, red blood cells count, hematocrits, serum iron, serum ferritin, and platelet counts were observed in the patient group compared to the healthy controls (P<0.01). Other parameters such as MCV, MCH and MCHC were not different between the two groups (P> 0.05, table 2).

Table 1 show s that 42% of patients were taking iron supplements. Therefore, we compared hematological parameters according to iron intake (table 3). The results showed no differences between the two groups in all examined parameters except hemoglobin, which was higher in the group who were taking iron supplements.

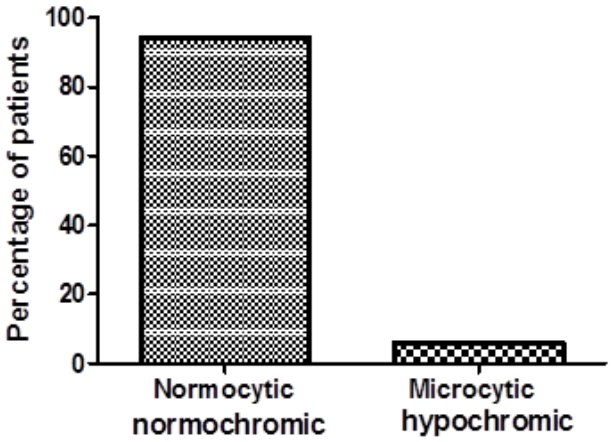

Fig. 1: Types of anemia among end stage chronic renal failure patients in Sudan.

DISCUSSION

In the current study, hematological parameters were examined in patients with chronic renal failure attending dialysis unit in Khartoum, Sudan. The results showed that most of the patients had anemia even that they were under erythropoietin therapy. In addition, no significant differences were observed in all hematological parameters between patients with or without iron supplements except for hemoglobin.

In the current investigation, about 98% of CRF patients who were attending dialysis units (end-stage disease) had anemia. Such high frequency is consistent with previous studies that was conducted in India (Singh, Aggarwal *et al*., 1999, Talwar, Gupta *et al*., 2002, Varma, Kumar *et al*., 1999), Nigeria (Akinsola, Durosinmi *et al*., 2000), Germany (Schiffl and Lang, 2006), Indonesia (Anees and Ibrahim, 2009), and Spain (Lepe-Zuniga, Morales-Molina *et al*., 2016). The results showed that normocytic normochromic anemia was the most common type while few were suffering from microcytic hypochromic anemia. This distribution is also consistent with most literature that indicate that normocytic, normochromic anemia is the typical type (Akinsola, Durosinmi *et al*., 2000, Anees and Ibrahim, 2009, Schiffl and Lang, 2006, Talwar, Gupta *et al*., 2002, Varma, Kumar *et al*., 1999).

All patients of the current investigation were under erythropoietin therapy. In the body, erythropoietin is produced by cells of the proximal convoluted tubule and it controls red blood cell formation from erythroid progenitor cells in the bone marrow (Zhang, Yang *et al*., 2017). Erythropoietin was suggested as a therapeutic agent to correct anemia in CRF patients (Paoletti and

Table 1: Characteristics of participants

Parameters	Control group (n = 30)	Patients group (n = 70)
Age in years	42.7 ± 12.4	46.8 ± 12.9
Gender (Male: female)	1 : 1	1.3 : 1
Iron Supplementation	0%	42%
Epo Supplementation	0%	100%
Anemia	0%	98.5%

Table 2: Hematological parameters among control and patients groups

Parameters	Control group (n = 30)	Patients group (n = 70)	P value
Hb (g/dl)	12.8 ± 1.2	8.5 ± 2.0	< 0.001
RBCs $\times 10^6$/µl	4.5 ± 0.4	3.07 ± 0.8	< 0.01
HCT (%)	39.9 ± 3.6	26.8 ± 6.3	< 0.001
MCV (fl)	87.0 ± 3.1	87.2 ± 5.0	0.8
MCH (pg)	28.5 ± 1.1	28.0 ± 1.8	0.06
MCHC (g/dl)	32.6 ± 1.0	31.8 ± 1.1	0.78
S. iron (µg/dl)	96 ± 20.6	62.4 ± 14.3	< 0.001
S. ferritin (µg/l)	72 ± 23.7	580 ± 99	< 0.001
TWBCs$\times 10^3$/µl	6.0 ± 1.5	5.63 ± 1.8	0.242
PLT$\times 10^3$/µl	238 ± 45.5	159.7 ± 52.7	< 0.001

Table 3: Hematological parameters among patients groups with or without iron supplementations

Parameters	Without Iron (n = 41)	With Iron (n = 29)	P value
Hb (g/dl)	8.17 ± 2.0	9.01 ± 1.8	0.048
RBCs $\times 10^6$/µl	2.95 ± 0.74	3.22 ± 0.78	0.141
HCT (%)	25.9 ± 6.3	27.92 ± 6.14	0.095
MCV (fl)	87.2 ± 5.5	87.3 ± 4.3	0.460
MCH (pg)	28.0 ± 1.8	28.2 ± 1.8	0.307
MCHC (g/dl)	31.8 ± 1.1	32.0 ± 1.0	0.447
S. iron (µg/dl)	56.02 ± 12.2	72.3 ± 11.6	< 0.001
S. ferritin (µg/l)	592 ± 93	558 ± 104	0.166
TWBCs$\times 10^3$/µl	5.6 ± 1.8	5.8 ± 1.7	0.587
PLT$\times 10^3$/µl	155 ± 50	169 ± 56	0.265

Cannella, 2006) and has been shown to improve hematological parameters in most patients with end stage CRF (Schmid and Schiffl, 2010).

The results showed no significant differences in the hematological parameters between patients with or without iron supplements except for hemoglobin and serum iron. Iron deficiency in CRF patients on dialysis is expected as some iron will get lost during dialysis and frequent blood sampling for laboratory examinations (Agarwal, 2017, Wittwer, 2013). It is estimated that patients on dialysis lose approximately one gram of iron per year. The lack of differences in most hematological parameters between patients with or without iron supplements indicates that iron is not central to the management of anemia in CRF patients on dialysis. A similar observation was reported in a previous study (Trivedi and Brooks, 2003) but not in another (Eschbach and Adamson, 1989). In general, iron supplements are recommended during erythropoietin therapy to prevent functional iron deficiency (Van Wyck, 1989).

In conclusion, the high prevalence of anemia among CRF patients on dialysis in Sudan highlights the need for the use of new treatment approaches. This might include hypoxia-inducible factor stabilizing compounds and prolyl hydroxylase inhibitors (Malyszko, 2014, Malyszko and Malyszko, 2016).

CONCLUSION

In conclusion, the majority of end stage CRF patients in Sudan (98%) had anemia with impairment in most of hematological parameters in spite of erythropoietin and iron therapy.

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REFERENCES

Agarwal R (2017). Iron deficiency anemia in chronic kidney disease: Uncertainties and cautions. *Hemodial. Int.,* **21**(Suppl 1): S78-S82.

Akinsola A, Durosinmi MO and Akinola NO (2000). The haematological profile of Nigerians with chronic renal failure. *Afr. J. Med. Med. Sci.,* **29**(1) 13-16.

Anees M and Ibrahim M (2009). Anemia and hypoalbuminemia at initiation of hemodialysis as risk factor for survival of dialysis patients. *J. Coll Physicians. Surg Pak.,* **19**(12) 776-780.

Collister D, Ferguson T, Komenda P and Tangri N (2016). The Patterns, Risk Factors and Prediction of Progression in Chronic Kidney Disease: A Narrative Review. *Semin Nephrol.,* **36**(4): 273-282.

Cosola C, Rocchetti MT, Cupisti A and Gesualdo L (2018). Microbiota metabolites: Pivotal players of cardiovascular damage in chronic kidney disease. *Pharmacol. Res.,* **130**: 132-142.

Dorgalaleh A, Mahmudi M, Tabibian S, Khatib ZK, Tamaddon GH, Moghaddam ES, Bamedi T, Alizadeh S and Moradi E (2013). Anemia and thrombocytopenia in acute and chronic renal failure. *Int. J. Hematol. Oncol Stem Cell Res.,* **7**(4): 34-39.

Eschbach JW and Adamson JW (1989). Guidelines for recombinant human erythropoietin therapy. *Am. J. Kidney Dis.,* **14**(2 Suppl 1): 2-8.

Gnudi L, Benedetti S, Woolf AS and Long DA (2015). Vascular growth factors play critical roles in kidney glomeruli. *Clin Sci (Lond)* **129**(12): 1225-1236.

Hsu RK and Powe NR (2017). Recent trends in the prevalence of chronic kidney disease: Not the same old song. *Curr Opin Nephrol Hypertens,* **26**(3): 187-196.

Kutuby F, Wang S, Desai C and Lerma EV (2015). Anemia of chronic kidney disease. *Dis. Mon.,* **61**(10): 421-424.

Lepe-Zuniga JL, Morales-Molina P and Garcia-Nandayapa GA (2016). [End stage renal disease lymphopenia; Characterization and clinical correlation]. *Rev. Med. Inst. Mex. Seguro Soc.,* **54**(4): 446-453.

Malyszko J (2014). New renal anemia drugs: is there really anything new on the horizon? *Expert Opin Emerg Drugs,* **19**(1): 1-4.

Malyszko J and Malyszko JS (2016). Emerging drugs for the treatment of kidney disease-induced anemia. *Expert Opin Emerg Drugs,* **21**(3): 315-330.

Paoletti E and Cannella G (2006). Update on erythropoietin treatment: Should hemoglobin be normalized in patients with chronic kidney disease? *J Am. Soc. Nephrol.,* **17**(4 Suppl 2): S74-S77.

Ramanath V, Gupta D, Jain J, Chaudhary K and Nistala R (2012). Anemia and chronic kidney disease: Making sense of the recent trials. *Rev. Recent Clin. Trials.,* **7**(3): 187-196.

Schiffl H and Lang SM (2006). Folic acid deficiency modifies the haematopoietic response to recombinant human erythropoietin in maintenance dialysis patients. *Nephrol. Dial Transplant.,* **21**(1): 133-137.

Schmid H and Schiffl H (2010). Erythropoiesis stimulating agents and anaemia of end-stage renal disease. *Cardiovasc Hematol. Agents Med. Chem.,* **8**(3): 164-172.

Singh NP, Aggarwal L, Singh T, Anuradha S and Kohli R (1999). Anaemia, iron studies and erythropoietin in patients of chronic renal failure. *J. Assoc Physicians India* **47**(3): 284-290.

Stel VS, Bruck K, Fraser S, Zoccali C, Massy ZA and Jager KJ (2017). International differences in chronic kidney disease prevalence: A key public health and epidemiologic research issue. *Nephrol. Dial. Transplant,* **32**(suppl 2) ii129-ii135.

Talwar VK, Gupta HL and Shashinarayan (2002). Clinicohaematological profile in chronic renal failure. *J. Assoc. Physicians India,* **50**: 228-233.

Torban E and Goodyer P (2009). The kidney and ear: emerging parallel functions. *Annu. Rev. Med.,* **60**: 339-353.

Trivedi HS and Brooks BJ (2003). Erythropoietin therapy in pre-dialysis patients with chronic renal failure: lack of need for parenteral iron. *Am. J. Nephrol.,* **23**(2): 78-85.

Van Wyck DB (1989). Iron management during recombinant human erythropoietin therapy. *Am. J. Kidney Dis.,* **14**(2 Suppl 1): 9-13.

Varma PP, Kumar R, Prasher PK and Roy ND (1999). Hypochromic anaemia in chronic renal failure-role of aluminium. *J. Assoc Physicians India,* **47**(7): 690-693.

Weisbord SD (2007). Symptoms and their correlates in chronic kidney disease. *Adv. Chronic Kidney Dis.,* **14**(4): 319-327.

Wittwer I (2013). Iron deficiency anaemia in chronic kidney disease. *J. Ren. Care,* **39**(3): 182-188.

Xu X, Nie S, Ding H and Hou FF (2018). Environmental pollution and kidney diseases. *Nat. Rev. Nephrol.,* **14**(5): 313-324.

Ye L and Mao W (2016). Metabonomic biomarkers for risk factors of chronic kidney disease. *Int. Urol. Nephrol.,* **48**(4): 547-552.

Zadrazil J. Horak P (2015). Pathophysiology of anemia in chronic kidney diseases: A review. *Biomed Pap Med Fac. Univ. Palacky Olomouc Czech Repub.,* **159**(2): 197-202.

Zhang C, Yang C and Zhu T (2017). From Erythropoietin to Its Peptide Derivatives: Smaller but Stronger. *Curr. Protein Pept. Sci.,* **18**(12): 1191-1194.