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The haematological profile of Nigerians with chronic renal failure

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Summary
In an attempt to add to existing sparse literature on the haematological profile in chronic renal failure (CFR) in Nígeria, we have undertaken a comprehensive haematologycal sturdy of 39 patients (male 27, female 12) age range 11-56yr., (mean 28.8 ± 11.8) who had established pre-dialytic CFR. The mean haematocrit was 24.1± 6.7%(range 12-40%). Severe anaemia was found in seven (18%), mild to moderate anaemia in 27 (69%) whilst five patients were not anaemic. Haematocrit correlated inversely with the degree of renal failure as assessed by serum creatinine ($r = -0.35$, $P < 0.05$). Red cell morphology was variable but the majority of patients showed a normocytic, normochromic blood film. Thę reticulocyte counts/indices were low. The mean total white cell count was generally within normal limits, ranging from (2 to 10.5 × 10^9/1) , with a mean of 5.3 ± 2.1× 10^9/1 and striking eosinophilia in 5 patients. Platelet count ranged between 82 and 350 × 10^9/1 (mean 156.5± 65.7 × 10^9/1) with only 3 patients having a relatively low count of <100 × 10/ 1.Prolonged bleeding time (BT) >9 minutes occurred in 13 (25.6%). There was no significant correlation between platelet count and bleeding time $r = 0.21$, $P = 0.34$. No significant correlation was observed between serum creatinine and bleeding time $r = 0.09$, $P > 05$.The bone marrow showed predominantly normocellular marrow but 7 patients had hypocellularity. Myeloid: Erythroid ratio ranged between 1:1 and 10:1, (mean 3:6:1) and correlated positively with serum creatinine values. ($r = 0.37$, $P = 0.048$). Bone marrow storage iron was absent in two and reduced in six patients. Severe anaemia is a common feature in Nigeria patients with CRF and it strongly associated with the severity of the renal failure. The low reticulocyte count and the tendency for erythroid hpoplasia to occur with increasing severity of renal failure would necessitate the use of erythropietin in our patients. The increased bleeding tendency in some of the patients calls for caution in surgical procedures in these patient.

Keywords: *Anaemia, chronic renal failure, uraemia, haemostatic failure, and bone marrow*

Résumé
Dans une tentative d'ajouter des elements de literature sur le profile haematologique chez les patients Nigerians souffrent d'insufisance renale chronique (CRF), nons avious enterpris an etude haema tologique comprehensive de 39 patients (27, males, 12 femmelles) ages de 11 a 56 ans (moyeme d'age 28,8±11,8) que avaient etablient ure CRF pre-dialiqtique. L'haematocrite moyenne etait de 211, 1±6.7% (ecart 12 a 40%). L'anemie severe avait ete identefier ches sept (18%) des patients, l'anemie legere a modereavait ete trouve chez 27 (69%) des patients, alorsque 5% des patients n'etaient pas anemi. L'haematocrite avait correle inversement avec le degree denseufisance renale detecte par le teste de serum creatine ($r = 0,35$, $P < 0.01$). La morphologie des globules ranges etait variable, mais la maforite des patients on monties des forties sanguins a normoaytes et monochronique. Le compte des reticulocytes/ indices etait faible. Laimoyene totale du compte des globules blaucs etait generalement dans les lime tes normales, et compris entre 2 et 10.5 x 10^9 I, avll more moyime de 5,3 ± 2, 1 x 10^9/l et une eosnphiliefrappante cez 5 patients. Le compte des platelettes sanguines etait compris entre 82 et 350 x 10^9/l (Moyenee 156, 5± 65, 7x10^9/ l) avle 3 per tients senlevient agant un failshe compte <100x 10^9/l. Le temps de signement prolange (BT) > gunites ete constate ches avait 13 patients (25.6%). Il n'y avait pas de correlation significative entre le compte de platelates et le temps de sigmement $r = 0,21$, $P = 0, 34$. aucune corrlection significative n'avait ete observee ntre le taux de cretine duplasma et le temps signement $r = 0, 09$ $P>0. 5$. La unqelle observe avait montre de un aviere predominante des normocellulaires, nais chez 7 patients il 'l a eu une hypercellularite. Le ratio myelide erythroide variait entre 1:1 a 10:1 (moyenne 3,6:1) et les valeurs on correle de positivement avec les tanx de creatine du plasma ($r = 0,37$, $P = 0, 048$). L'accumulation de fer dans la moellc obsure atait asente on reduite cheze 6 et 2 des patients respectivements. L'aneuine serve est un trait cammun chez les patients Nigeiran. Souffrant de la CRF et elle est fortement associe a la serve rete de l'nisufisance renale. Le faible corrpte de reticulocyte et la tendance de l'hypophasis des erythroides de survenires avc la se erite de l'insufisance renale necessiterail lintilisation de l'erythropoietine chez nos patients. La tendance crossante se signement chez certains des patients appelle a ha pru dence dans les procedure chirurgicales chez les patients.

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Introduction

Anaemia and haemostatic abnormalities are well recognised consequences of chronic renal failure and when severe; they certainly worsen the prognosis in the patient [1,2,3]. Efforts directed at improving the anaemia with the use of recombinant erythropoietin has improved the quality of life in CRF patients while dialysis therapy has equally improved uraemic bleeding [4,5]. Although the haematological profile has been described in many centers outside Africa, there are only a few publications devoted to the topic in the, West African literature [6]. The dramatic burst of renal activities in Nigeria leading to the increase in the number of dialysis centres has compelled an appraisal of some of the parameters that directly influence quality of life in patients with CRF. The peculiar circumstances of the tropics such as social economic and

environmental factors and differences in the causative factors may impose differences in the haematological profile of these patients.

Materials and methods

Patients in established CRF, as defined by serum creatinine levels consistently above 266 umol/1 and ultrasonographic parameters of reduced renal mass and/or poorly defined cortico-medullary differention, and increased parenchymal echogenicity were identified.[7] Only those who had not received haemodialysis or peritoneal dialysis were randomly selected for study. Patients were on dietary regimen and fluid therapy with no added folate or iron therapy at least 6 weeks prior to the study [8]. The daily intake of protein, calories, sodium, and potassium were 30-40 g (mainly of high biological value), at least 3000 cal; 40-60 mmol; and 20-40 nmol. Respectively. Exclusion criteria were blood transfusion within the preceding three months, very ill patients requiring urgent dialysis and those with haematological diseases, particularly sickle cell anaemia, that could primarily affect haematological profile.

All patients had a detailed history and physical examination aimed at determining the aetiological factors and the severity of the renal failure. Serum creatinine and renal ultrasonography were done to further evaluate the severity of the disease. Five millilitres of venous blood collected and anticoagulated in EDTA for haematological parameters using standard operating procedures [9]. Such parameters included: haematocrit (Hct), total white cell count and differentials, platelet count, blood film appearance, reticulocyte count/ index, haemoglobin elcetrophoresis and glucose-6-phosphate dehydrogenase (G6PD) screening. Another 5ml of venous blood was anticoagulated in lithium heparin for measurement of plasma creatinine in the routine laboratory. Bleeding time was obtained using Ivy's method [10], and bone narrow aspiration biopsy from the sternum was undertake with patient's consent.

Blood and fixed marrow films were stained using Leishman's stain. These films were observed for morphology of the cells. Other fixed marrow films were stained with Perl's stain graded for the presence or absence of iron as follows:

Absent	0	No stainable iron
	1+	small iron particles just visible in reticulum cells using oil objective
Reduced	2+	small, sparse iron particles in reticulum cells visible at a lower power
Adequate	3+	Numerous small particles in reticulum cells
	4+	Larger particles with a tendency to aggregate into clumps
	5+	Dense, large clumps
	6+	Very large clumps and extracellular iron [11]

Statistical analysis

Absolute figures and / or means ± standard deviation (SD) of the parameters measured are stated while the comparison of means was done with Mann-Whitney- U test. The relationship between variables especially the severity of renal failure and haematological parameters were determined using simple linear regression.

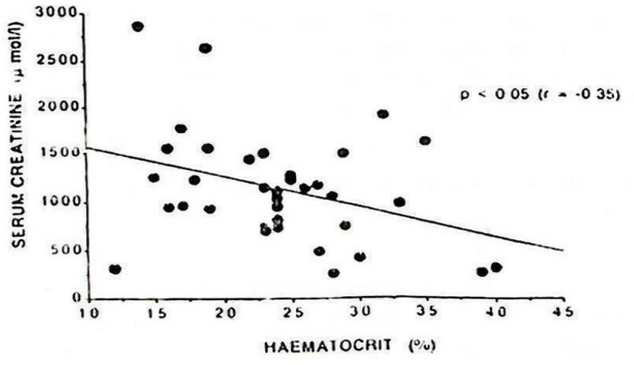
Results

Table 1: Haematological parameters of patients with chronic renal failure.

Parameters	Range	Mean	SD	Normal Range
Age (yrs)	11-58	28.8	±11.8	
Haemtocrit (%)	12-40	24.1	± 6.7	Male 47±7 Female 42± 5
WBC (x10⁹/1)	2-10.5	5.3	±2.1	2-11
Platelets (x 10⁹/1)	82-350	156.5	±65.7	90-400
Bleeding Time (min)	3.5-30	8.1	±5.5	3-9
Serum Creatinine (µmol/1)	266-2892	1130	576	50-110
Myeloid: Erythroid (M:E) ratio.	1:1 -101	3.6:1		3-4:1

Table 1 shows the means and standard deviation of the various parameters studied. Thirty-nine patients, comprising in 27 males and 12 females aged between 11 and 56 years, with a mean age of 28.8 ± 11.8 years participated in the study.

CRF was attributable to chronic glomerulonephritis in 16 (41%), hypertensive disorder in 14(35 %) adult polycystic kidney disease in one (2.6%) and other unclassifiable diseases, being a combination of conditions including diabetes mellitus, hypertension and proteinuria in eight (20.5%). Serum creatinine ranged from 26 to 2,8925. µmol/l, with a mean value of 1130.3 ± 5767 mol/l. The haematocrit ranges from 12-40%, means 24.1 ± 6.7%. Severe anaemia (Hct < 18%) occurred in seven (18%), moderately severe anaemia (Hct between 26 and 35%) in (28%) whilst five (13%) patients were not anaemic. The reticulocyte count / index ranged between less than 1 and 2%. There was a significant inverse correlation ($r = -0.35$, $P < 0.05$) between haematocrit value and the severity of renal failure as assessed by serum creatinine (Fig.1).



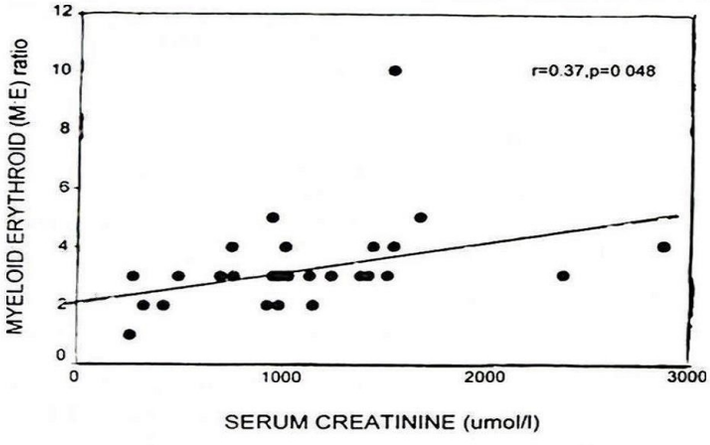
The relationship between serum creatinine and haematocrit showing a significant negative correlation

Blood films showed a varying degree in red cell morphology, with the majority of patients showing a normochromic picture and 11 showing moderate anisopiokilocytosis and hypochromia.

The total white cell count was within normal range between 2 and 10.5x 10/1, with a mean of 5.3 ± 2.1 x 10/1. White cell different count was as follows; neutrophils ranged between 16 and 90%.(mean of 57 ± 20%); lymphocytes 10-63% (mean of 33 ±13%) and eosinophilia 12±15%. The mean abslute eosinophil count was 0.65 ± 1.35 x 109/1. Five patients had eosinophilia with counts ranging between 1.0 and 5.9 x 109/1. This was associated with loaisis in one patient. A relative neutrophil leucocytosis occurred in 3 patients with neutrophil ranging between 75 and 90% of total WBC.

Platelet counts ranged from 82 to 350 x 10^9/1, with a mean of 156.5 ± 65.7x109/1. Values below 100 x 10^9/1 were obtained in 3 patients. Bleeding times ranged from 3.5 to 30 minutes with a mean of 8.1 ± 5.5 minutes. Prolonged bleeding (> 9 minutes) occurred in 13 (25.6%) patients. No significant correlation was observed between serum creatinine and bleeding time (r = 0.09, $P > 0.05$. There was also no significant correlation between platelet counts and bleeding time. r = 0.21, $P = 0.34$. Bone marrow examination was possible in 32 patients seven of whom showed hypocellularity whilst the others were normcellular. The myeloid/erythroid (M:E) ration ranged from 1:1 to 10:1 with a mean of 3:6:1. M:E ratio significantly correlated positively with the degree of renal failure as defined by serum creatinine. (r = 0.37,P = 0.048) Fig. 2.

Fig.2 Relationship of M:E ratio and Serum creatinine



Bone marrow storage iron was adequate in **21 (65.6%)**, reduced in 6 (18.7%), negative in 2 (6.2%) but technically difficult to assess in 3 (9.4%) .Megakaryocytic were present in adequate amount except in 3 patients in whom they were reduced. G6PD activity was deficient in two of the 11 patients in whom it was assessed.

Discussion

Anaemia is a frequent finding in patients with established CRF and the degree is influenced by the underlying disease, the severity of renal failure and sometimes the mode of treatment [1,12 -15]. The finding of anaemia of varying severity in majority of our patients is in agreement with observations of other workers in this part of the world [6]. Many factors have been incriminated in the etiology of the anaemia of CRF. These include bone marrow hypoplasia, increased red cell destruction, increased tendency to bleed, while reduced erythropoietin production and uraemic toxins have been considered fundamentally responsible [12,-16]. A significant inverse relationship was observed in this study, between haematocrit and serum creatinine, which is in agreement with the findings of other researchers [14,15], thus indicating that the severity of the renal failure is an important factor in the pathogenesis of anaemia in this condition. However, the one marrow hypocellularity in some patients and prolonged bleeding time (> 9 min) in some others might have contributed to the anaemia. Generalised bone marrow hypoplasia reported by Oluboyede and Williams [6], was not observed in this study as the majority of patients had normocellular marrow. In spite of this, however, it was observed that the higher the M.E ratio the worse the uraemia as reported by Gallen and Limarzi [17]. This suggests that patients with severe disease have a tendency to have erythroid hypoplasisa and may, therefore, benefit from erythropoitin therapy. The total white cell count of patients in the present study was within normal range for the general population in this environment. [18] Neutropenia (absolute neutrophilia count < 1000/ cmm) was not seen in any patient, which confirms that the bone marrow hypoplasia observed here, did not affect the granulocyte series. On the contrary, relative neutrophilia was found in a few patients but without hypersegmentation of neutrophils as observed by Jaleel et al. [19]. The cause of the relative neutrophilia was not investigated, however, infection may have a role to play . Eosinopilia (absolute count >1000/cmm was not common and when it occurred it was associated with parasite infestation.

Haemostatic failure has been described in CRF and is attributed largely to uraemia induced platelet dysfunction [2,20]. The observation of mild thrombocytopaenia (platelet count < 100 x 109/1) in only 3 patients and yet a disproportionately large number of 13 patients having prolonged bleeding would suggest that platelet dysfunction could occur in the presence of a normal platelet count. A similar observation was reported by Panicucci *et al.* [21] who also observed that bleeding disorders due to thrombocytopaenia may occur only at levels lower than 50 x 10^9/1. In the present study, we did not observe a significant correlation between bleeding time and severity of CRF as assessed by serum creatinine and thus BT could not be used to predict the severity of CRF and this is in agreement with the observation of Castaldi *et al.* [22].

Bone marrow storage iron was used to assess the iron status of patient in this study, rather than serum ferritin (an acute phase protein,) transferrin and total iron building capacity because of limited resources. The observation of reduced or absent storage iron in up to 25% of patients, in this study , is in agreement with that of Odutola *et al.* [23] but contrasts with data from Eschbach and Adamson [12]. Iron supplements should thus be recommended to patients with blood films showing evidence of iron deficiency irrespective of the severity of CRF. The contribution of G6PD deficiency to anaemia in the patients in whom it occurred was probably negligible but its presence calls for caution with the use of drugs that may provoke haemolysis. Only a few patients were screened for G6 PD activity, a major limitation to the interpretation of this finding.

References

1. Ersley AJ. Anaemia of chronic renal disease. Arch Intern Med 1970; 126:774-780.
2. Hotton RA and Oshen MJ. Haemostatic mechanism in uraemia. J Clin Path 1968; 21: 406-411.
3. Klahr saulo. Anaemia, Dialysis and Dollars. N Eng. J.of Med 1996; 334: 461-463.
4. Valderrabona F. Recombinant erythropoetin: 10years of clinical experience. Nephrol Dial Transplant 1997; 12 (suppl,1) : 2-9.
5. Daniel Daykin. Uraemic blessing. kidney Int. 1983: 24 ; 698 - 705.
6. Oluboyede OA and Williams AIO. Serum ferritin and other iron indices in adult Nigerians with chronic renal failure Afr. J. Med. & med. Sci. 1995; 24: 231-237.
7. Akinsola A, Odesanmi WO, JO Ogunniyi and GO A Ladipo. Disease causing chronic renal failure in Nigeirans. A prospective study of 100 cases. Afri.J. Med & med Scs. 1989; 18: 131 -137.
8. Akinsola A, Smith IF T, Alimi F and Odewale and G OA Ladipo *et al*: Low protein/high calorie dietary regimen in renal failure, A preliminary study of Nigeiran patients. Afri.J. Med. & med Scs. 1991; 20:53-59.
9. Bain BJ Basic Haematological Techniques. In: Practical Haematolofy; 8th edition eds Dacie J V and S .M Lewis, Churchill Livingstone. Edinburgh. 1995; 49-97.
10. Laffan M.A and A E Bradshaw. In: Practical Haematology: 8th edition eds Dacie J V and S M Lewis, Churchill Livingstone, Edinburgh. 1995; 318-319.
11. Bain B J 1992. Normal bone marrow. In Bone marrow pathology. Blackwell Scientific publications, Oxford,. 29.
12. Eschbach JW, Adamson JW. Anaemia of end stage renal disease. Kidney Int. 1985; 28 (1): 1-5.
13. Eschbach JW, Egrie JC Downing MR, Browne JK and Adamson JW. Correction of anaemia of end stage renal disease with recombinant human erythropoetin. Results of a combined phase 1 and 2 clinical trial. N. Eng.J Med. 1987; 3 16:73-78.
14. Delwiche F, Segal G M, Eschbach JW, Adamson JW. Haemopoetic inhibitors in chorinic renal failure. Lack of in vitro specificity. Kidey Int. 1986; 29: 641-648.
15. Radtke HW, Klalussner a Erbes PM, Scheuerman EH, Schoppe W, Koch KM; serum erythpoeitin concentration in chronic renal failure: relationship to degree of anaemia and excretory renal function. Blood 1979; 54: 877-884.
16. Livio M. Benigni A, Remuzzi G: Coagulation abnormalities in uraemia. Semin. Nephrol 1985; 5: 82-90.
17. Callen IR and LR Limarzi. Blood and bone marrow studies in renal disease Am J. Clin Path., 1950. 20: 3-23.
18. Ukaejiofor EO, Isaacs - Sodeye WA; Adigun S and A. Ipadeola. Normal haematological values in adult Nigeirans. NMJ 1979; 9: 117-119.
19. Jaleel S, Roberta F, Richard MF Folic acid, hypersegsmented polymorphonucler leucocytes and the uraemic syndrome. AMJ. Clin Nutrition 1970; 23: 1-16.
20. Horowitz H I Uraemic toxins and platelet function. Arch Intern Med 1970; 126: 823-826.
21. Panicucci F. Sagripanti A Prinori E, Vispi M, Lecchini L, Barsotti G, Giovannetti S. Comprehensive Study of haemostasis in chronic uraemia: Nephron 1983; 33: 5-8.
22. Castaldi PA, Homeostasis and Kidney disease. In Disoders of Homeostaos. Eds Ratnoff and Forbes C D. Grune & Stratton, Orlando. 1994; 473 - 483.
23. Odutola TA, Ajose - Coker OO, Mabadaje AFB, OAOluboyede. Serum ferritin and other Iron indices in adultNigerians with chronic renal failure. N M J. 1987; 103-107.