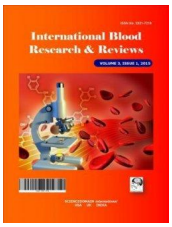

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# Haematologic Profile of Patients with Chronic Kidney Disease in Port Harcourt, South-South Nigeria

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***Authors' contributions***

*This work was carried out in collaboration between all authors. Authors EIO and OAE designed the study. Author EIO wrote the protocol and wrote the first draft of the manuscript. Authors EIO and OCP managed the literature searches and analyses of the study. Authors EIO and RIOJ performed the statistical analysis. All authors read and approved the final manuscript.*

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## ABSTRACT

**Aim:** The objective of this study is to assess the haematological profile of our patients with chronic kidney disease.
**Study Design:** This was a cross-sectional case-control study.
**Place and Duration of Study:** University of Port Harcourt Teaching Hospital, Rivers State Nigeria 2015.
**Methodology:** A total of 186 subjects with chronic kidney disease (CKD) were enrolled at the University of Port Harcourt Teaching Hospital (UPTH); among these, 124 subjects had received

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more than one unit of blood within one month or more than ten units of blood within three months. The remaining 62 CKD subjects (control population) have never been transfused. Complete blood count, serum creatinine and urea levels were determined for all participants. Estimated GFR (eGFR) was calculated using the abbreviated Modification of Diet in Renal Disease (MDRD) formula.

**Results:** The red cell count, haemoglobin, haematocrit and red cell indices were decreased in all the study participants with chronic kidney disease. The mean haemoglobin, haematocrit and red cell count were found to be significantly lower in the multiply transfused patients compared to the non-transfused patients. Serum creatinine showed negative correlation with red cell count, haemoglobin and haematocrit in the study population.

**Conclusion:** The study shows that anaemia was present in all subjects, and was inversely proportional to the severity of chronic kidney disease in this setting.

*Keywords: CKD; transfusion; full blood count; creatinine; eGFR.*

## 1. INTRODUCTION

Chronic kidney disease (CKD) is a major public health concern globally, with a greater proportion of the disease burden in developing countries [1]. In 1990, there were 409,000 deaths due to CKD and it increased to 956,000 in 2013 [2,3]. Uraemia in chronic kidney disease (CKD) is said to interfere with erythropoiesis, leucocyte, thrombocyte, and general immune functions [3].

Thus CKD patients are prone to anaemia, recurrent infections and bleeding tendencies [3]. End-stage renal disease (CKD stage 5) is defined as glomerular filtration rate (GFR) of less than 15 mls/min per 1.73 $m^2$, which is often accompanied by clinical features of uraemia [2,4]. CKD patients have been reported to have lower haematological indices due to impaired erythropoietin (EPO) production, reduced lifespan from uraemic poisoning, bone marrow suppression, haematuria and gastrointestinal haemorrhage [5].

Anaemia is the commonest haematological complication of CKD and worsens with deterioration of renal function [5,6]. According to the World Health Organization (WHO) criteria, anaemia is diagnosed in males and post-menopausal women when haematocrit is less than 39%, and in non-pregnant/pre-menopausal females when haematocrit is less than 36% [7].

Although there are multiple mechanisms involved in the pathogenesis of anaemia of chronic kidney disease, the primary cause is the diminished production of erythropoietin by the diseased kidney [7,8]. Erythropoietin is produced in the peritubular cells of the kidney and is the major hormone involved in red cells synthesis [8]. Low levels of erythropoietin lead to production of diminished number of oxygen-carrying red cells [9]. Anaemia causes decreased oxygen delivery to the tissues, leading to diminished exercise capacity, cognitive impairment and diminished quality of life [8].

Anaemia in CKD has also been implicated in the development of left ventricular hypertrophy and congestive heart failure which may be fatal if untreated [9]. The degree of anaemia in CKD appears to be roughly proportional to the severity of the renal failure [8,9,10].

The anaemia of CKD is typically normochromic and normocytic and there may be mild reticulocytosis [5]. They are, however, seen less frequently in other cases of CKD especially in hypertensives [9]. The effects of uraemia on leucocytes include a decrease in phagocytic activity, impairment of complement activation by the haemodialysis membrane (leading to leucostasis in the pulmonary circulation) and a temporary leucopaenia [10]. There is a decrease in cell-mediated immunity thereby predisposing CKD patients to recurrent infections but a better graft survival [5]. The study was carried out to assess basic haematological parameters in adult Nigerians with end-stage renal disease at the University of Port Harcourt Teaching Hospital, Port Harcourt, in Southern Nigeria.

## 2. METHODOLOGY

### 2.1 Study Design

This was a cross-sectional case-control study carried out at the University of Port Harcourt Teaching Hospital (UPTH), Port Harcourt, South-South Nigeria.

## 2.2 Ethical Consideration

Ethical approval was obtained from the UPTH Ethics Committee before commencement of the study. Informed written consent was obtained from each patient before recruitment into the study.

## 2.3 Study Population

The study population consisted of 186 adult patients with chronic kidney disease defined by patients who have GFR >60 ml/min/1.73 $m^2$ for ≥3 months[1], calculated using the modified diet in renal disease (MDRD) formula who had received multiple whole blood transfusion (more than one unit of blood within one month) or more than ten units of blood within three months, and adult patients with chronic kidney disease with no history of blood transfusion [11]. The study population were recruited consecutively within a three-month period from the nephrology outpatient clinic, medical outpatient clinics, as well as medical inpatients (with CKD) in UPTH.

### 2.3.1 Inclusion criteria for the cases

Patients with CKD were enrolled into the study if they were eighteen years and above, and had received multiple whole blood transfusions (more than one unit of blood within one month).

### 2.3.2 Exclusion criteria for the cases

Patients with chronic kidney disease who are HIV positive, and/or had septicaemia or ulcers or other proven causes of anaemia other than primarily CKD, and/or those with a history of kidney transplant.

### 2.3.3 Inclusion criteria for the controls

Patients with chronic kidney disease who are eighteen years and above; who have never been transfused.

### 2.3.4 Exclusion criteria for the controls

Patients with chronic kidney disease who have had a kidney transplant; and those who are HIV positive.

## 2.4 Specimen Collection

Five millilitres of venous blood were collected, dispensed into EDTA Vacutainer® bottles and analysed within four hours for full blood count (haemoglobin, haematocrit, and red cell indices which included mean cell volume, mean cell haemoglobin and mean cell haemoglobin concentration), platelet count, total white cell count and differentials. The analysis was carried out using a 3-part auto-analyzer (Sysmex model Kx21N). Haematocrit was regarded as low if 30 L/L or less for adult females, 33 L/L or less in adult males. Platelet count was considered to be low if 90 x $10^9$/L or less. The normal reference range of total white cell count was taken as 4.0 – 10.0 x $10^9$/L [12].

## 2.5 Data Collection

The values for serum urea and creatinine were obtained from patient's hospital data records.

The estimated glomerular filtration rate (eGFR) was calculated using the abbreviated modified diet in renal disease (MDRD) formula.

$$eGFR\ (mL/min/1.73\ m^2) = 186.3 \times (Serum\ Cr\ (\mu mol/l))^{-1.154} \times (age)^{0.203} \times 1.212\ (if\ patient\ black) \times 0.742\ (if\ female)$$

## 2.6 Data Analysis

Data was summarized by appropriate statistical tools such as mean, median, standard deviation; frequencies and proportion. The t-test was used to compare differences between two groups. All tests were carried out at a 95% confidence interval; p-value of ≤0.05 was considered significant. The Pearson's moment correlation was used to test the relationship between creatinine level and eGFR in the subjects. The SPSS v20 (IBM, USA) statistical package was used to analyse all data.

## 3. RESULTS

A total of 186 participants with chronic kidney disease were recruited into the study. They comprised of 124 patients with a history of multiple blood transfusions and 62patients without a history of blood transfusion (used as controls).

The multiply transfused CKD patients and the non-transfused CKD patients were well-matched for sex and age as shown in Table 1.

Among the multiply transfused patients, the mean serum creatinine and urea was 906.2 (±631.2) µmol/l and 28 ± 9.8 mmol/l respectively compared to 608.9 ± 392.9 mmol/l and 20.4 ± 12.4 mmol/l for the non-transfused (control)

patients. The differences in serum creatinine and urea in the transfused and non-transfused were statistically significant as shown in Table 2. The mean estimated GFR for multi--transfused patients was 24 mls/min/1.73 $m^2$ compared to 36 mls/minute/1.73 $m^2$ for controls (without a previous history of blood transfusion). This value was statistically significant, p-value <0.0001.

### 3.1 Haematological Profile of Patients with Chronic Kidney Disease

The mean haematocrit for the multiply transfused patients was 22.2 ±9.5 L/L while the mean haematocrit for the non-transfused patients was 27.1 ±7 L/L. Multiply transfused patients had a red cell count of 2.3 ± 0.9 x $10^9$/L compared to 2.8 ± 0.7 x $10^9$/L in non-transfused patients. The values for haematocrit and red cell count were all statistically significantly lower for the multiply transfused patients compared to the non-transfused ($p$<0.001), as shown in Table 3.

Mean MCH, MCHC and MCV for multi-patients were 26.2 ±2.6 pg, 30.1 ±2.6 g/dl and 74.8 ±4.2 fl respectively. For the non-transfused, the mean MCH, MCHC and MCV were 29.1 ±2.3 pg, 31.1 ±4.3 g/dl and 79.1 ±6.8 fl, respectively. The respective differences in the values of MCH, MCHC and MCV between these groups were not statistically significant, as shown in Table 3.

Multiply transfused patients had a median total white cell count of 9.4 x $10^9$/L compared to 8.2 x $10^9$/L in the non-transfused patients; the difference here was not statistically significant ($p$ value = 0.416). The absolute neutrophil and lymphocyte counts in both subgroup of patients (multiply transfused vs non-transfused) did not also show any statistical significance, as shown in Table 3. Similarly, the difference in mean platelet count in multiply transfused patients and non-transfused patients was statistically significant ($p$ = 0.031), as shown in Table 3.

Figs. 1 and 2 shows a negation correlation of haemoglobin and creatinine in the transfusion naïve and multiply transfused subjects respectively.

## 4. DISCUSSION

On assessment of the haematological profile of patients with chronic kidney disease (CKD), the mean haematocrit and red cell count for the multiply transfused CKD were respectively found to be significantly lower compared to that of non-transfused. This is consistent with some studies which reported that impaired erythropoietin secretion in CKD was directly associated with a decrease in red cell count and subsequent reduction in the haematocrit level [13,14]. An inverse relationship has been shown to exist between stable-state haematocrit and glomerular filtration rate in patients with chronic kidney disease; this is said to reflect severity of chronic kidney disease [15].

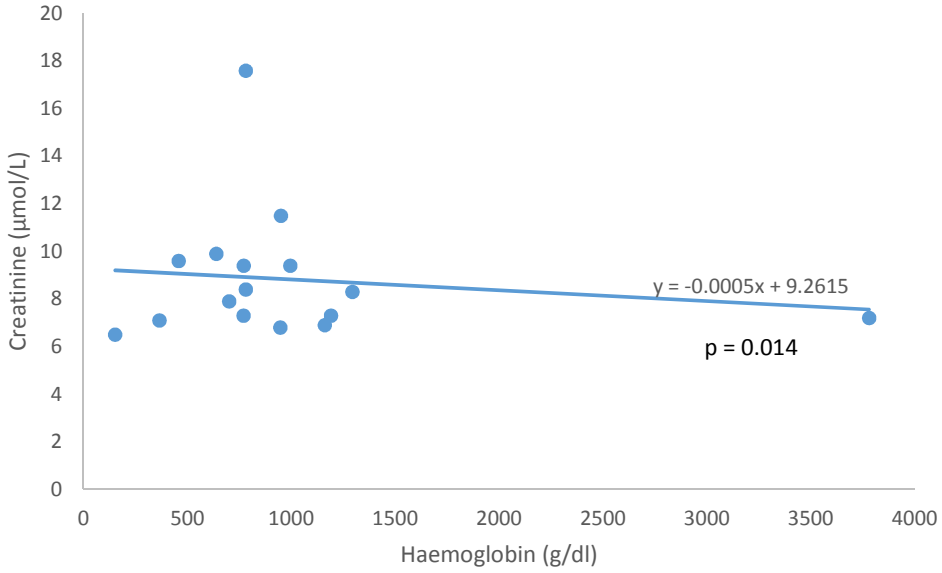


**Fig. 1. Correlation analysis of creatinine and haemoglobin in transfusion-naïve CKD patients**

**Table 1. Age and sex distribution of patients with chronic kidney disease (CKD)**

| Age range (years) | Multiply transfused ESRD patients. (n =124) | | Non-transfused CKD patients. (n =62) | |
|---|---|---|---|---|
| | Male (n/%) | Females (n/%) | Male (n/%) | Female (n/%) |
| <20 | 5(7.4) | 0 | 0 | 0 |
| 20-29 | 7 (10.3) | 9 (16.1) | 2 (5.3) | 3 (12.5) |
| 30-39 | 6 (8.8) | 15(26.8) | 7 (18.4) | 5 (20.8) |
| 40-49 | 20 (29.4) | 7 (12.5) | 14 (36.8) | 9 (37.5) |
| 50-59 | 14 (20.5) | 13 (23.2) | 2 (5.3) | 3 (12.5) |
| >60 | 16 (23.5 | 12 (21.4) | 13(34.3) | 4 (16.6) |
| Total | 68 (100.0) | 56 (100.0) | 38 (100.0) | 24 (100.0) |

**Table 2. Biochemical characteristics of the study subjects**

| Variable | Non-transfused CKD patients | Multiply transfused CKD patients | p-value |
|---|---|---|---|
| Creatinine (µmol/L) | 608.9 ± 392.9 | 906.2 ± 631.2 | <0.0001* |
| Urea (mmol/L) | 20.4 ± 12.4 | 28 ± 9.8 | <0.0001* |
| eGFR (mls/mins/1.73 $m^2$) | 36 | 24 | <0.0001* |

*eGFR: Estimated glomerular filtration rate, Values are expressed as mean ± SD, *Indicates difference is statistically significant (p<0.05)*

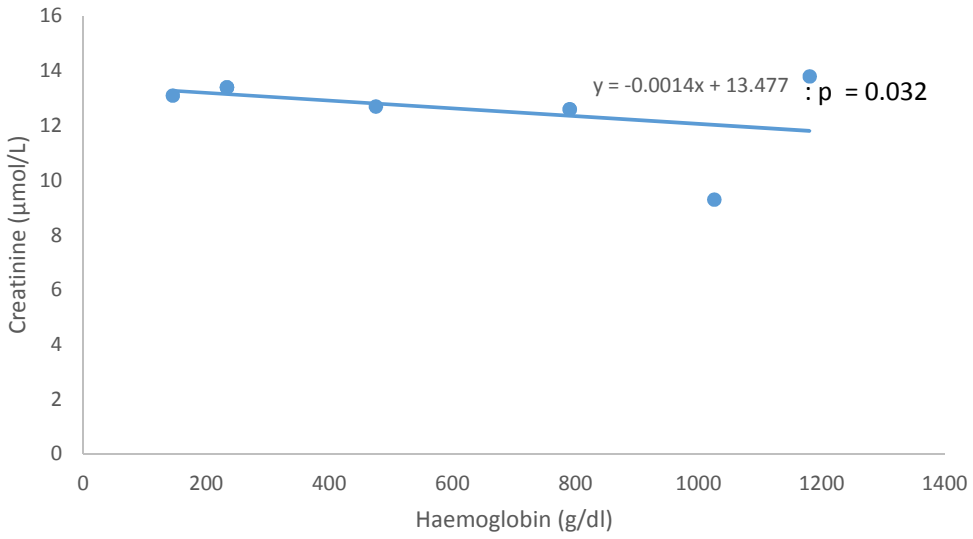


**Fig. 2. Correlation of creatinine and haemoglobin in multi--transfused patients**

In this study, the multiply transfused patients were found to be in a more severe stage of renal impairment, had lower levels of haematocrit, lower red cell count and lower haemoglobin concentration compared to the non-transfused control population. This implies the likelihood of greater transfusion requirements in patients in the later stage of CKD. Studies have also an increase in the transfusion requirement in patients who develop CKD as a complication of the existing diseased conditions such as sickle cell anaemia [16]. Multiple blood transfusions may have mid- to long-term adverse effects, and should be applied cautiously as it is known that the risk of immunization against red blood cells increases with the number of transfusions [17].

The MCV, MCH and MCHC were within normal ranges similar to the reports of other studies in Nigeria [6,14,15]. Normocytic normochromic anaemia is usually observed in CKD, similar to that of most chronic disorders, except in the presence of other associated factors like nutritional deficiencies, malaria, chronic haemorrhage, drug toxicity among others [5,9].

**Table 3. Haematological profile of study population**

| Variable | Non-transfused CKD patients | Multiply transfused CKD patients | *P*-value |
|---|---|---|---|
| Haemoglobin concentration (g/dl) | 8.6 ± 2.3 | 7.2 ± 1.6 | < 0.001* |
| Haematocrit (L/L) | 27.1 ± 7.0 | 22.2 ± 9.5 | < 0.001* |
| Red cell count (x $10^9$/l) | 2.8 ± 0.7 | 2.3 ± 0.9 | <0.001* |
| Mean cell haemoglobin concentration (g/dl) | 31.1 ± 4.3 | 30.1 ± 2.6 | 0.134** |
| Mean cell haemoglobin (pg) | 29.1 ± 2.3 | 26.2 ± 2.6 | 0.340** |
| Mean cell volume (fl) | 79.1 ± 6.8 | 74.8 ± 4.2 | 0.401** |
| Platelet count (x $10^9$/l) | 230.3 ± 107 | 190.6 ± 107.4 | 0.031* |
| Absolute granulocyte count (x $10^9$/l) | 7.8 ± 6.8 | 5.5 ± 3.3 | 0.805** |
| Absolute lymphocyte count (x $10^9$/l) | 3.8 ± 5.4 | 3.6 ± 4.3 | 0.822** |
| Median total white cell count (x $10^9$/l) | 9.4 | 8.2 | 0.416** |

*Values are expressed as mean ± SD, *Indicates difference is statistically significant (p<0.05)*
***Indicates difference is not statistically significant (p>0.05)*

The median total white cell count was within normal range in both those with and without a previous history of blood transfusion, similar to reports from some studies [6,14,18]. The mean platelet counts for the multiply transfused and non-transfused patients were within normal range. This might be because thrombopoietin is mainly produced in the liver [18]. However, they were significantly lower in the multiply transfused compared to the transfusion-naïve patients; anti-platelet immunization may have a role here [19].

Normal leucocyte and platelet counts in CKD are not unusual observations, as uraemia affects the function of leucocytes and platelets rather than their production. Thus CKD patients may be prone to infections and haemorrhage despite normal leucocyte and platelet counts [5,6,11,14].

## 5. CONCLUSION

There were significant changes in basic haematological indices of patients with CKD with or without previous blood transfusion. These changes were found to be more profound in the multiply transfused CKD patients.

## CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

## ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the authors.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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