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# Monitoring Frequency of Haemoglobin, Calcium and Phosphorus and the Impact on Correction in Patients on Maintenance Haemodialysis in Douala-Cameroon

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## Abstract

**Background:** There is scarcity of data on the actual frequency of routine blood work-up for patients on maintenance haemodialysis and how this affects the achievement of therapeutic goals in sub-Saharan Africa. This study aimed to review these in a referral hospital in Cameroon. **Methods:** A prospective hospital-based cohort study carried out from November 2019 to April 2020 including patients on maintenance haemodialysis in Douala general hospital. Patients were followed during 6 months to determine the frequency of monitoring of haemoglobin, serum calcium and phosphorus. Targeted values for haemoglobin were ≥10 g/dL, 80 - 100 mg/L for serum calcium and 25 - 45 mg/L for serum phosphorus. Pearson correlation test was used to define the correlation between monitoring frequencies and blood values at the end of the study. **Results:** For all 154 patients included in the study, the median frequency of monitoring for haemoglobin was once every 8 week (IQR: 6 - 12) and once every 12 weeks (IQR: 8 - 24) for serum calcium and phosphorus. The proportion of patients who achieved haemoglobin, serum calcium and phosphorus targets at the end of the study were 27.4%, 63% and 74% respectively. No correlation was found between the frequency of monitoring and the haemoglobin, serum phosphorus and calcium levels at the end of the study.

**Conclusion:** The frequency of monitoring of serum haemoglobin, calcium and phosphorus by patients in this study was low with a high prevalence of patients not achieving target value.

## Keywords

Monitoring, Haemoglobin, Phosphorus, Calcium, Haemodialysis, Douala

## 1. Background

Kidney failure (KF) is a common outcome of chronic kidney disease (CKD) and is associated with high morbidity, high cost of treatment, poor quality of life, and high mortality making it a significant global public-health problem [1] [2] [3]. Management of KF is done mainly through kidney replacement therapy (KRT) of which haemodialysis (HD) is the main modality worldwide [1]. Patients on maintenance haemodialysis (MHD) experience numerous complications, including anaemia and chronic kidney disease-mineral and bone disorders (CKD-MBD) [4] [5] [6]. These complications are the cause of more than half of deaths among patients with KF due to the cardiovascular changes they bring about such as: cardiac hypertrophy, increased vascular thickness and accelerated arteriosclerosis [4] [5] [6]. Therefore, regular blood work-up is an important component of care for patients with KF [7]-[12].

Clinical practice guidelines for patients on MHD recommend routine monitoring of serum haemoglobin, calcium and phosphorus levels every 1 to 3 months to ensure proper control of anaemia and CKD-MBD [7] [8]. However, despite its perceived importance, no definitive evidence to support a specific interval of routine laboratory sampling has been brought forward [7] [8]. In Cameroon, the prevalence of CKD is estimated at 10% - 13.2% and the majority are referred to the nephrologists late in need of emergency dialysis [13] [14] [15] [16] [17]. Anaemia is common in CKD patients with a prevalence estimated at 79% amongst patients on MHD, requiring correction through frequent blood transfusions or erythropoiesis-stimulating agents (ESA) alongside close monitoring [18]. The median yearly out-of-pocket expenditure for HD in Cameroon was estimated at about XAF 2,420,300 ($4114), of which XAF 123,930 ($214) represented the cost of laboratory tests [19]. As a low-income country however, these costs of management and laboratory examinations are out of the reach of many patients who are usually unemployed or retired and live on less than XAF 1471 ($2.5) per day [20] [21].

Most haemodialysis centres in Cameroon recommend monthly monitoring of haemoglobin and serum calcium/phosphorus in patients on MHD, a recommendation whose effects have never been studied to the best of our knowledge. We aimed in this study to report on the frequency of monitoring of haemoglobin, serum calcium and phosphorous level in patients on MHD in a tertiary re-

ferral hospital in Cameroon and determine the association between monitoring frequency and the achievement of recommended targets.

## 2. Material and Methods

### 2.1. Study Setting

This study was conducted in the HD unit of the Douala General Hospital (DGH), which is the main referral hospital for patients with kidney diseases in the Littoral region whose chief town, Douala serves as the commercial and economic capital of Cameroon. The unit comprises 2 nephrologists and 2 general practitioners. The centre was equipped with 21 Fresenius haemodialysis generators, used synthetic polysulfone dialysis membrane and bicarbonate dialysate. The centre operated from Monday to Saturday and offered to each registered patients 2 dialysis sessions of 4 hours duration each per week. Patients are routinely prescribed a monthly biological work-up that comprises a full blood count, serum phosphorus and serum calcium. These monthly control exams are given at a discount when executed together in the hospital-owned laboratory but may be done elsewhere. Consultations to the attending physicians can be done from Mondays to Fridays and is free of all charges. Administrative authorization was obtained from the DGH and the study was approved by the University of Bamenda Ethics Committee (No.: 2020/0237H/UBa/IRB).

### 2.2. Study Design

This was a hospital-based prospective cohort study carried out from November 2019 to April 2020.

### 2.3. Data Collection

All adults (≥18 years old) patients who provided a written informed consent and have been on haemodialysis for at least 3 months from the start of the study were recruited. All patients who died or left the HD centre before the end of the study were excluded. For each patient a pre-tested questionnaire was used to collect the required information under the assistance of a final year undergraduate medical student. The questionnaire included socio-demographic (age, sex, level of education and monthly income), clinical characteristics (comorbidities, presumed aetiology of KF, vascular access used, duration on dialysis), and paraclinical (monthly haemoglobin, serum calcium and phosphorus levels when available) over the 6 months duration of the study.

### 2.4. Definition of Operational Terms

Targeted goals of haemoglobin were set at ≥10 g/dL while those of serum calcium and phosphorus were set at ranges 80 - 100 mg/L and 25 - 45 mg/L respectively.

The recommendations on the routine monitoring in the HD centre were at least monthly monitoring of all three parameters.

Frequency of monitoring was calculated using the formula: [24/(*number of controls done*)] and expressed as a weekly interval.

### 2.5. Statistical Analysis

Data collected was analysed using the Statistical Package for Social Services (SPSS) v23.0. Continuous variables were presented as means and standard deviations, medians, interquartile ranges and percentages. Categorical variables were summarized using counts and percentages. Correlation between the monitoring frequencies and the values obtained at the end of the study were examined using the Pearson correlation coefficient test. A p-value of <0.05 was considered statistically significant.

## 3. Results

### 3.1. Baseline Profile of Patients

A total of 172 patients on MHD were on maintenance haemodialysis at the beginning of the study among which 17 died before the end of the study and 1 was lost to follow up. A total of 154 participants (93 males and 61 females) were therefore included in the final analysis. The overall age of participants ranged from 20 to 77 years with a mean of 50.2 ± 13.5 years. Overall, 57.1% (88/154) of patients were unemployed, 59.1% (91/154) depended on family and friends as their main source of funding and 6.5% (10/154) had a health insurance. Hypertension (90.3%), diabetes mellitus (15.6%) and HIV (6.5%) were the main comorbidities whereas hypertension (31.2%), chronic glomerulonephritis (14.9%) and diabetes mellitus (11.0%) were the leading baseline nephropathies. The median HD vintage was 33 months (IQR: 16 - 71). Most of the participants used an arterio-venous fistula as vascular access for HD 96.1% (148/154) and received twice haemodialysis session per week 97.4% (150/154) (see **Table 1**).

### 3.2. Management of Anaemia and Serum Calcium and Phosphorus Disorders

Correction of anaemia was done mostly through blood transfusions 49.4% (76/154) with 27.3% (42/154) making use of erythropoietin at least once during the study. About 30.5% (47/154) received neither erythropoietin nor blood transfusions. Vitamin D supplementation and phosphate binders were used respectively by 29.9% (46/154) and 37.7% (58/154) of participants at least once during the course of the study (**Table 2**).

### 3.3. Frequency of Haemoglobin, Serum Calcium and Phosphorus Blood Monitoring

The median monitoring frequency of haemoglobin was every 8 weeks (IQR: 6 - 12) with only 8.4% (13/154) doing controls at the recommended 4-week intervals. The median frequency of monitoring of serum calcium and phosphorus was every 12 weeks (IQR: 8 - 24). The proportion of participants who performed

**Table 1.** Baseline characteristics of participants.

| Variables | Overall |
|---|---|
| Mean age, yr (SD) | 50.2 (13.5) |
| Age, min-max, yr | 20 - 77 |
| **Gender, n (%)** | |
| Male | 93 (60.4%) |
| Female | 61 (39.6%) |
| **Monthly income (XAF)** | |
| Unemployed | 88 (57.1%) |
| <50,000 | 13 (8.4%) |
| 50,001 - 100,000 | 20 (13%) |
| 100,001 - 150,000 | 13 (2.6%) |
| 1,500,001 - 200,000 | 4 (10.4%) |
| >200,000 | 16 (8.4%) |
| Insurance | 10 (6.5%) |
| **Haemodialysis vintage (months)** | |
| Median (IQR) | 33.0 (16 - 71) |
| **Vascular access, n (%)** | |
| AV fistula | 148 (96.1%) |
| Central venous catheter | 6 (3.9%) |
| **Comorbidities, n (%)** | |
| Hypertension, | 139 (90.3%) |
| Diabetes mellitus | 24 (15.6%) |
| HIV positive | 10 (6.5%) |
| **Aetiology of KF, n (%)** | |
| Hypertension | 48 (31.2%) |
| Chronic glomerulonephritis | 23 (14.9%) |
| Diabetes mellitus | 17 (11.0%) |

SD: Standard deviation; HIV: Human immunodeficiency virus; IQR: Interquartile range; KF: Kidney Failure.

**Table 2.** Pharmacological management of anaemia and serum phosphorus and calcium disorders.

| Variables | Total n (%) |
|---|---|
| **Correction of Anaemia** | |
| Blood transfusions | 76 (49.4) |
| Oral Iron | 53 (34.4) |
| IV Iron | 51 (33.1) |
| ESA | 42 (27.3) |
| Neither ESA nor transfusion | 47 (30.5) |

**Continued**

| | |
|---|---|
| **Correction of calcium and phosphorus disorders** | |
| Use of phosphate binders | 58 (37.7) |
| *Calcium carbonate* | 51 (33.1) |
| *Sevelamer carbonate* | 7 (4.5) |
| Vitamin D | 46 (29.9) |
| *Native* | 34 (22.1) |
| *Active* | 12 (7.8) |

ESA: Erythropoiesis stimulating agents.

monitoring of serum calcium and phosphorus at the recommended frequency was 1.3% (2/154) and 33.1% (38/154) performed every 24 weeks (Figure 1).

As shown in Figure 2, there was a significant decline in the proportion of participants achieving the target levels of haemoglobin over time from 40.8% to 13.8% by week 24 (Figure 2). Overall, only 27.4% of participants were on average within the desired haemoglobin range, giving us a prevalence of anaemia of 72.6%. We observed slight increases in the number of participants achieving the desired serum calcium and phosphorus levels over time, with an average of 63.0% and 74.3% respectively (Figure 2).

### 3.4. Correlation between Monitoring Frequencies and Monitored Parameters

In this study, no significant correlation was found between the frequency of monitoring of haemoglobin ($r = 0.064$; $p = 0.635$), phosphorus ($r = 0.369$; $p = 0.11$) and serum calcium levels ($r = -0.192$, $p = 0.416$) (see Table 3).

## 4. Discussion

In this 6-month prospective cohort study on patients on MHD, receiving care in one of the main haemodialysis centres of Cameroon, the percentage that adhered to clinical guidelines of haemoglobin and serum calcium/phosphorus monitoring frequency was 8.4% and 42% respectively. Less than one-fifth of patients were within desired therapeutic ranges of haemoglobin at the end of the study which was significantly lower than the numbers recorded at the start. No correlation was found between the frequency of monitoring of haemoglobin, phosphorus and serum calcium levels and their serum values by the end of the study.

There is little evidence for the optimal frequency of routine blood work-up monitoring for patients on HD therapy and this is especially true in SSA. The Kidney Disease Improving Global Outcomes (KDIGO) anaemia guideline recommends haemoglobin measurement at least monthly in patients with KF on MHD [8]. The KDIGO CKD-MBD guidelines recommend serum calcium and phosphorus measurements every 1 to 3 months [7]. However, the strength of the recommendations is "not graded" [8]. Patients on MHD in our study setting are

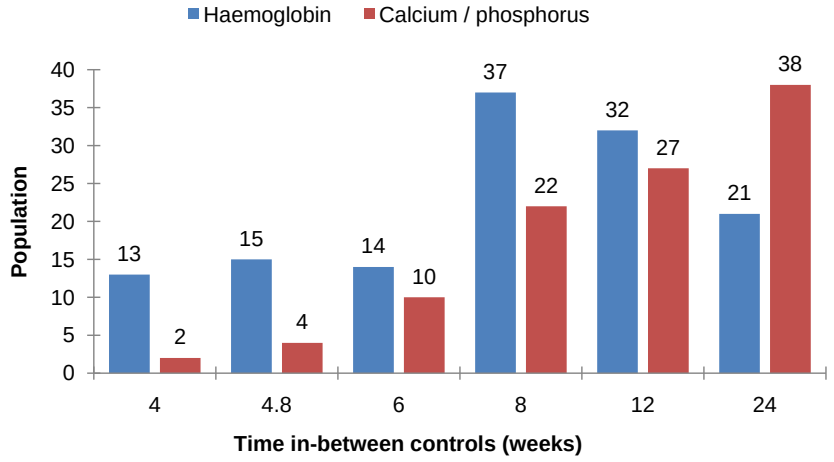


**Figure 1.** Monitoring frequencies of haemoglobin, calcium and phosphorus.

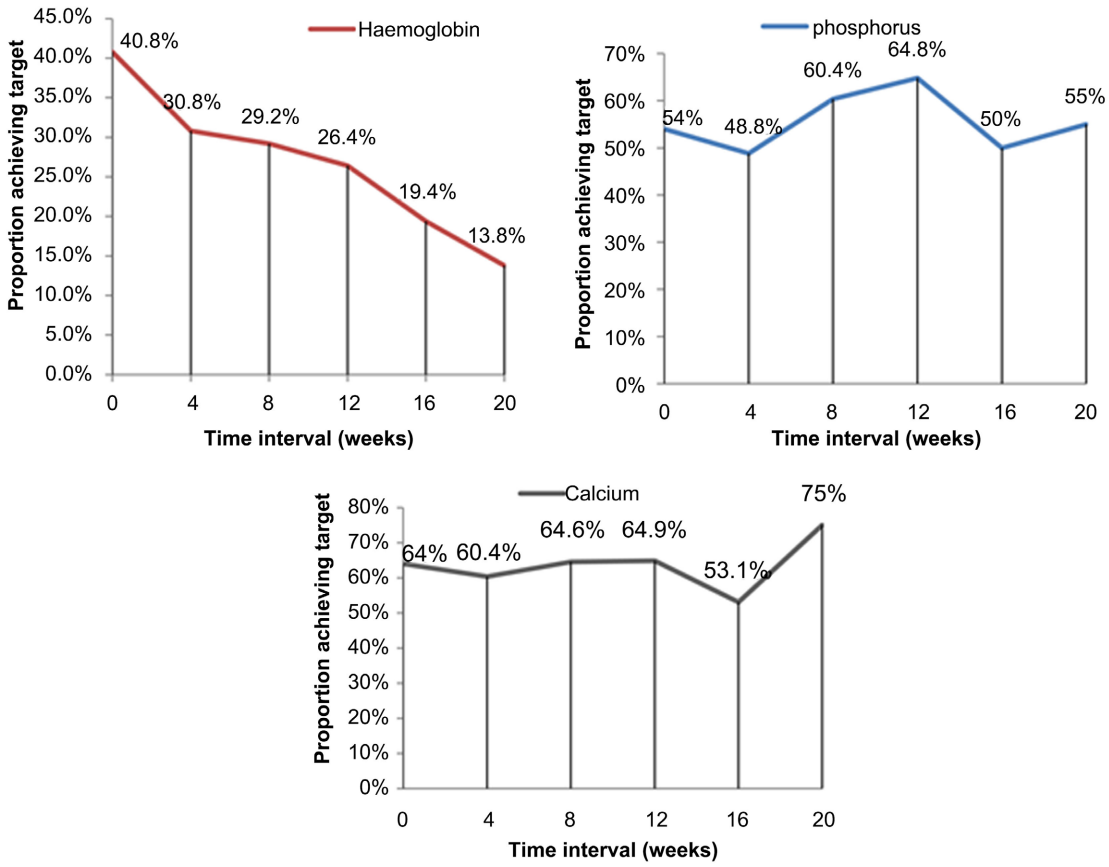


**Figure 2.** Attainment of therapeutic targets of haemoglobin (upper left panel), phosphatemia (upper right panel) and calcemia (lower panel) amongst participants over the course of the study.

**Table 3.** Correlation between monitoring frequency and controlled parameters.

| | | Serum Haemoglobin levels | Serum Phosphorus levels | Serum Calcium levels |
|---|---|---|---|---|
| Monitoring frequency | Pearson's correlation | 0.064 | 0.369 | 0.192 |
| | p-value | 0.635 | 0.110 | 0.416 |

recommended to control serum haemoglobin, calcium and phosphorus levels monthly. We found the median monitoring frequencies of haemoglobin and serum calcium/phosphorus were below all recommendations [7] [8]. These low frequencies could be explained by the high financial burden of these tests on an already overburdened population as all these tests are out-of-pocket payments. More than half (57.1%) of our study population were unemployed and only 12.5% had a medical insurance. A previous study in the country reported a high median annual cost of dialysis than is out of reach of most patients [19]. Despite government subsidies on dialysis sessions, other costs such as drugs, laboratory and radiologic testing, hospitalisations etc. are completely borne by patients and their families [19].

Although the proportion of patients who performed surveillance of haemoglobin in a given month remained mostly constant, the proportion of those within the therapeutic target declined consecutively every month, with an average target achievement for the overall duration of the study of 27.4%. These results were higher than the 12.2% reported by Maïz *et al* in Tunisia [22]. One explanation for this higher value in our study could be the difference in the defining thresholds for anaemia with higher haemoglobin targets in the study by Maïz *et al.* (≥12 g/dL). In addition, fewer patients in that study were on ESA therapy (10.8%) as compared to ours (27.3%). However, our results were still well below the values demonstrated by Silver *et al.* in Canada who reported 60% patients achieving haemoglobin level targets, (10 - 12 g/dL) [23]. This difference can be explained by the low proportion of patients that were on ESA in our study (27.3%) as opposed to that by Silver *et al.* (78%). The poorer haemoglobin control in our study is in line with the literature that suggests that ESA use is associated with better control of anaemia and reduced haemoglobin variations as opposed to blood transfusions [12] [24].

The proportion of participants who achieved target values of serum calcium and phosphorus was 63.0% and 74.3% respectively. These results were almost similar to those of Abderraman *et al.* in Senegal in 2015 (63.7% and 60.9% respectively) [25]. Possible explanations for these low rates are; first the high level of non-adherence to dietary restrictions in our setting as reported by Musaga *et al.* [26] and secondly, the low use of oral phosphate binders, with only 37.7% of our participants using it throughout the study.

We didn't find a statistically significant relationship between the monitoring frequencies of haemoglobin, serum calcium and phosphorus and the serum values achieved after 6 months of follow up. However, this doesn't explicitly conclude in a lack of relationship between these two variables and we cannot refute the assertion that monitoring frequencies positively affects therapeutic results. We speculate our non-significant results were due either to a low statistical power resulting from a modest sample size or, the relationship is being moderated by other variables not measured in the present study such as the different corrective therapies, their availability and timely use. While it is also plausible to suggest there exist no cause-effect relationship between monitoring frequency and con-

trol of anaemia and phoshocalcic imbalances from our results, the existence of previous studies such as the study by Khan *et al.* in the United States in 2011 [27] who concluded that more frequent Hb monitoring (weekly vs. monthly) and timely ESA dose adjustments were associated with better haemoglobin control and the study by Yokoyama *et al.* in Japan [28] demonstrating that more frequent (weekly) monitoring of calcium and monthly monitoring of PTH levels were associated with achievement of guideline recommended targets, are prove no effect existing is unlikely.

### Study Strengths and Limitations

This was a single centre study with a limited sample size and based on health records. It is however of note that there has been an effort to prospectively collect data in a standardized fashion which limited the potential effects of missing data. Certain parameters were not recorded, such as physician prescription and patient's timely compliance which may have had an effect on the correction of anaemia and CKD-MBD as well as being an important confounding factor in the correlation tests. Despite the aforementioned limitations, our study has its strengths; there is limited data on the actual monitoring frequency of these blood parameters by patients on MHD in SSA as well as its effects on proper follow-up. To the best of our knowledge this will be the first study of its kind in the country and will help lay the grounds for further research on the topic thereby raising awareness on the importance of regular laboratory workup amongst patients, clinicians and policy makers.

## 5. Conclusion

The frequency of haemoglobin, calcium and phosphorus monitoring remains below what is expected. This was associated with poor control of anaemia and CKD-MBD, with the proportion of patients who achieve desired therapeutic ranges of haemoglobin decreasing with time. Studies to better identify the reasons for this low monitoring frequency will need to be carried out and patients need to be sensitized on the importance it has in the management of their disease.

## Authors' Contribution

**HMP**: Study conception and design, supervision of data collection and analysis, drafting of the manuscript, **KTOL**: data collection and analysis, drafting of the manuscript; **TMA**: Data analysis, critical revision of the manuscript; **SBF**: supervision of data collection and analysis, critical revision of the manuscript; **FH;** supervision of data analysis, critical revision of the manuscript. **AEG:** Study conception and design, critical revision of the manuscript. All authors read and approved the final manuscript.

## Ethics Approval and Consent to Participate

Ethical approval was obtained from the Bamenda University Ethics Committee

and consent to participate was obtained from each patient.

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## Conflicts of Interest

The authors declare that they have no competing interests.

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## Abbreviations

**DGH:** Douala General Hospital;
**CKD:** Chronic Kidney Disease;
**CKD-MBD:** Chronic Kidney Disease-Mineral and Bone Disorder;
**HD:** Haemodialysis;
**KDIGO:** Kidney Disease Improving Global Outcomes;
**KF:** Kidney Failure;
**KRT:** Kidney Replacement Therapy;
**SD**: Standard Deviation;
**SSA**: Sub-Saharan Africa.