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Prevalence and Predictors of Malnutrition in Patients with Chronic Kidney Disease Stages 3 – 5 non Dialyzed

Prévalence et facteurs prédictifs de la malnutrition chez les patients en insuffisance rénale chronique stades 3 – 5 non dialysés

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Mots clés : malnutrition, MRC non dialysée, SGA, facteurs prédictifs, Afrique sub-saharienne.

ABSTRACT

Objective. This cross-sectional study was designed to evaluate the nutritional status of non-dialyzed chronic kidney disease (CKD) patients and to identify predictive factors of malnutrition in this population. **Methods.** Consenting non-dialyzed CKD patients aged above 21 years who consulted at the out-patient nephrology unit of the Yaounde General Hospital (YGH), from December 2013 to March 2014 were eligible. Patients with acute intercurrent illnesses, malignancy, or prosthetic devices were excluded. Relevant clinical data was recorded. Laboratory, anthropometric and bioelectric impedance parameters of interest were evaluated. Nutritional status was assessed using the Subjective Global Assessment (SGA) questionnaire. Multivariate regression analysis was used to determine predictors of malnutrition. **Results.** A total of 72 (42 males) were included in the study. Their mean (standard deviation) age was 56.22 (11.80) years. The median (interquartile range, IQR) estimated glomerular filtration rate (eGFR) was 17.00 (10.50 – 30.50) ml/min/1.73 m^2, with 41.7% of patients in CKD stage 5. The most frequent etiologies of CKD were hypertension (30.6%) and diabetes (23.6%). The median (IQR) protein intake was 1.02 (0.71 – 1.35) g/kg/day. The prevalence (95% confidence interval) of malnutrition was 38.9 % (27.3% – 50.0%). In multiple regression analysis, only low eGFR was an independent predictor of malnutrition. Bioimpedance and anthropometric parameters were not predictive of malnutrition. **Conclusion.** Malnutrition was common in CKD patients. A low eGFR was an independent predictor of malnutrition. These findings highlight the importance of nutritional assessment and intervention in the care of non-dialyzed CKD populations especially those with stage 5 CKD.

RÉSUMÉ

Objectif. Evaluer l'état nutritionnel des patients atteints de maladie rénale chronique (MRC) non dialysés et identifier les facteurs prédictifs de malnutrition dans cette population. **Méthodologie.** Etude transversale portant sur des patients atteints de MRC non dialysés, âgés de plus de 21 ans suivis à l'Hôpital Général de Yaoundé (HGY) de décembre 2013 à mars 2014. Des données cliniques, biologiques, anthropométriques et de la bioimpédance étaient recueillies. L'état nutritionnel a été évalué à l'aide du questionnaire "Subjective Global Assessment" (SGA). L'analyse multivariée était utilisée pour déterminer les facteurs prédictifs de la malnutrition. **Résultats.** Nous avons recruté 72 patients (42 hommes) avec un âge moyen de 56,22 ± 11,80 ans. Le débit de filtration glomérulaire estimé (DFGe) médian (intervalle interquartile, IIQ) était de 17,00 (10,50 - 30,50) ml/min/1,73 m^2, avec 41,7 % des patients au stade 5 de la MRC. Les étiologies les plus fréquentes de la MRC étaient l'hypertension (30,6 %) et le diabète (23,6 %). L'apport protidique médian (IIQ) était de 1,02 (0,71 - 1,35) g/kg/jour. La prévalence (intervalle de confiance à 95 %) de la malnutrition était de 38,9 % (27,3 % - 50,0 %). En analyse multivariée, seul un DFGe bas ressortait comme facteur prédictif indépendant de la malnutrition. Il n'y avait pas d'association entre les paramètres anthropométriques, de bioimpédance et la malnutrition. **Conclusion.** La malnutrition est fréquente chez les patients atteints de MRC. Le DFGe bas est le facteur prédictif indépendant de la malnutrition. Ces résultats témoignent de l'importance de l'évaluation et de la prise en charge nutritionnelle des patients atteints de MRC en particulier au stades 5.

INTRODUCTION

Protein energy wasting (PEW) also known as malnutrition is frequent in patients with chronic kidney disease (CKD) especially in the dialysis population where it adversely affects outcomes [1]. It is estimated that 40% of patients suffer from PEW at the time of initiating hemodialysis [2]. However, there is a dearth of data on the nutritional status of CKD populations in Sub-Saharan Africa.

Two single center studies in the hemodialysis population in Cameroon revealed a high prevalence of malnutrition at 47.7 % and 55 % respectively [3,4]. Whether these patients enter the hemodialysis program already malnourished is unknown. Furthermore, evaluation of nutritional status is not usual care in the CKD population in our setting. The aim of this study was to evaluate the nutritional status of non-dialyzed Cameroonians with CKD stages 3 through 5 to identify predictive factors of PEW in this population.

METHODS

Study setting and participant

This cross-sectional study was conducted at the out-patient nephrology unit of the Yaounde General Hospital (YGH), from 1st December 2013 to 31st March 2014. Consenting non-dialyzed CKD stages 3 -5 patients aged above 21 years were enrolled. Patients with acute intercurrent illnesses (severe infections, hepatic and cardiac failure), malignancies, or prosthetic devices were excluded. Limb-amputated patients were also excluded.

Procedures

We enrolled participants consecutively as they presented for routine nephrology outpatient consultations. Relevant clinical, anthropometric and bio-impedance data was obtained at inclusion. Nutritional status was assessed on the same occasion. Participants were again seen after 48hours to present a 48 hours meal frequency diary, a 24 hours urine sample for evaluation of urea excretion and for the collection of a fasting venous blood sample for relevant laboratory assays.

Nutritional status: we used the 7-point Subjective global assessment (SGA) questionnaire to evaluate nutritional status [5], which was classified as follows: A=normal nutritional status, B=mild to moderate malnutrition and C= severe malnutrition.

Daily protein intake and frequency of protein consumption: we estimated daily dietary protein intake from 24-hour urinary urea excretion using the Maroni formula [6]. The frequency of protein consumption was derived from a 48 hours meal diary. Protein foods referred to meat, poultry, seafood, dried seeds. Milk and other dairy products were considered separately.

Anthropometric measurements: Patient was undressed without shoes to perform the measurements. Skinfold thickness was measured with a HARPENDEN® caliper at three sites (triceps, biceps, sub scapular area) on the non-dominant arm of patients. The mid-arm muscle circumference (MAMC) was derived from the triceps skinfold thickness (TSF) and mid-arm circumference (MAC) as follows: MAMC = MAC - (3.14 x TSF). The height and weight were measured with a SECA® scale, and height gauge.

Bioelectrical impedance vector analysis was performed in all subjects using Bodystat® QuadScan 4000, to measure fat mass, lean body mass, body cell mass, lean dry mass.

Laboratory Assays: blood urea, serum creatinine, lipid profile, C-reactive protein (CRP), serum albumin, serum bicarbonate and hemoglobin and 24-hour urea excretion were the laboratory data of interest. All laboratory measurements were performed on the Hitachi/Cobas C 311machine (Roche, Germany, 2013). Serum creatinine was measured by the Jaffe alkaline picrate method, serum bicarbonate by phosphoenolpyruvate carboxylase test, CRP by immunoturbidimetry, serum albumin by the bromocresol purple method, serum lipids by colorimetric enzymatic method and urinary urea by enzymatic method. The estimated glomerular filtration rate (eGFR) was calculated using the 4-variables MDRD equation. Urinary protein excretion was estimated semi-quantitatively by urine dipsticks in a random urine specimen.

We estimated dietary protein intake from 24-hour urea excretion by the Maroni formula [6].

Ethics approval was provided by the Institutional Review Board of Yaounde General Hospital.

Statistical analysis

We used the Epi Info version 3.5.4 software to analyze the data. The student t-test and the Mann-Whitney (depending on the normal distribution or not of the variable) were used for comparisons between two groups for continuous variables. The chi-squared test and fisher exact test where appropriate for qualitative variables. Differences between more than two groups were assessed by analysis of variance (ANOVA).

Multivariate regression analysis was used to determine predictors of malnutrition. The level of statistical significance was set at a p value < 0.05.

RESULTS

Characteristics of the study population

A total of 72 (42 M) out of the 91 eligible patients, were enrolled in the study (**Figure 1**). Their mean (Standard deviation, SD) age was 56.22 (11.80) years and the median (interquartile range, IQR) estimated glomerular filtration rate (eGFR) was 17.00 (10.50 – 30.50) ml/min/ 1.73 m^2; with 41.7% (n=30) in stage 5 CKD. About 39% (n = 28) had diabetes and 18.1% (n=13) were obese, and, 61.1% (n = 44) had >1+ proteinuria on dipsticks. The median (interquartile range) duration of nephrology care was 4 (0 – 16) months, and 38.9% (n = 28) participants were on their first nephrologist visit (**Table I**). Only 11 patients (15.3%) had been prescribed a CKD specific diet, by a nephrologist. About 53% of participants (n = 38) had 2 meals a day, while 45.8% (n=33) had 3 meals a day. The frequency of protein consumption varied with meal and the median (IQR) of protein intake was 1.02 (0.71 – 1.35) g/kg/day. The mean (SD) values of anthropometric, bioimpedance and laboratory parameters are shown in **Table II**. Twenty-seven (37.5%) participants had a C-reactive protein ≥ 6mg/dl.

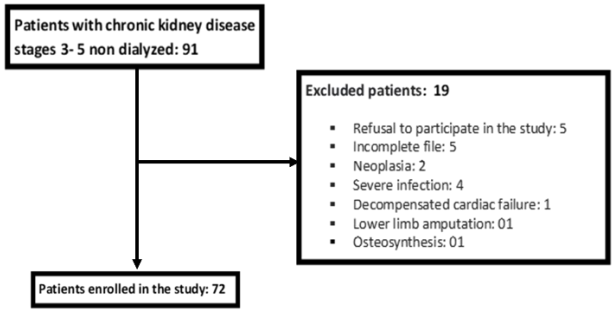

Figure 1. Flow-chart of the selection of participants

Table I: Characteristics of Chronic kidney disease

Variables	Frequency (N=72)	Percentage (%)
Stages of CKD		
Stages 3	19	26.4%
Stage 4	23	31.9%
Stage 5	30	41.7%
Duration of nephrology care		
Median (IQR)(months)	4.0	0.0 6.0
<1month	28	38.9%)
1- 3months	5	6.9%
≥3 months	39	54.2%
Comorbidities		
Hypertension	70	97.2%
Diabetes	28	38.9%
Hyperuricemia	20	27.8%
Obesity	13	18.1%
HCV	8	11.1%
HBV	5	6.9%
HIV	3	4.2%
Proteinuria		
<1+	28	38.9%
1+	19	26.4%
2+	9	12.5%
≥3+	16	22.2%

Abbreviations: CKD, Chronic Kidney Disease; HCV, Hepatitis C Virus; HBV, Hepatitis B Virus; HIV: Human Immunodeficiency Virus

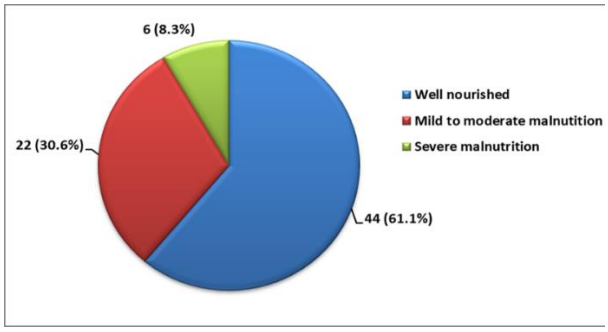

Figure 2. Prevalence and severity of Malnutrition

Prevalence and severity of malnutrition

The prevalence (95% confidence interval) of malnutrition was 38.9 % (27.3% – 50.0%), and increased with severity of CKD from 10.5 % in stage 3 to 70 % in stage 5 **(Figures 2 & 3)**. Over 8.3% of participants had severe malnutrition **(Figure 2)**.

Table II: Anthropometric, bioimpedance and laboratory parameters

Variables	Mean ± standard deviation
Anthropometric measurements	
Weight (kg)	74.3 ± 15.6
Height (cm)	165 ± 8
BMI (Kg/m^2)	27.0 ± 4.9
BMI <23 kg/m^2, n (%)	17 (23,6%)
MAC (cm)	29.4 ± 4.1
TSF (mm)	15.2 ± 9.2
MAMC (cm)	24.7 ± 3.0
Bioimpedance parameters	
Fat Mass (FM) (Kg)	18.1 ± 9.9
%Fat Mass	24.0 ± 10.6
Lean body mass (LBM)(Kg)	56.6 ± 14.4
%Fat Free Mass (FFM)	75.9 ± 10.7
Lean dry mass (LDM) (Kg)	11.6 ± 3.9
Body cell mass (BCM) (Kg)	34.5 ± 8.5
Laboratory data	
Blood urea(g/l)	1.2 ± 0.8
Serum creatinine (median, IQR) (mg/l)	36 (25.3 – 66.5)
Hemoglobin (g/dl)	9.6 ± 2.2
Anemia, n (%)	30 (51.7%)
Total cholesterol (g/l)	1.81 ± 0.49
Hypercholesterolemia, n (%)	20 (27.8%)
Serum bicarbonate (mmol/l)	26.1 ± 5.4
Metabolic acidosis, n (%)	14 (19.4%)
Triglycerides (g/l)	1.18 ± 0.67
Serum albumin (g/l)	37.8 ± 5.5
Hypoalbuminemia, n (%)	14 (19.4%)

Abbreviations: BMI, Body Mass Index; MAC, TSF, Tricipital Skin Fold; MAMC, Mid-Arm Muscle Circumference; MAC, Mid-Arm Circumference

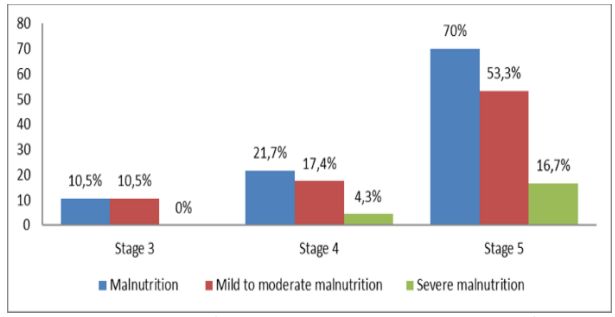

Figure 3. Prevalence of malnutrition according to Stage of CKD

Table III: Association between malnutrition and anthropometric and bioimpedance indices (simple logistic regression)

Variables	ß	Standard Error	p-value
Body mass index (Kg/m^2)	- 0.08	0.05	0.15
Triceps skinfold thickness (mm)	- 0.06	0.03	0.08
Mid arm muscle circumference (cm)	0.07	0.08	0.42
Fat Mass (Kg)	- 0.06	0.03	0.07
Lean body mass (Kg)	0.001	0.02	0.96
Lean dry mass (Kg)	- 0.06	0.06	0.32
Body cell mass (Kg)	- 0.01	0.03	0.76

Table IV: Predictive factors of malnutrition in patients with chronic kidney disease stages 3- 5 ND (simple and multiple regression analysis)

Variables	Malnutrition n (%)	OR (95% CI)	p-value	Adjusted OR (95% CI)	Adjusted p-value
Age					
≥ 50 years	15 (34.1)	0.34 (0.12 – 1.00)	0.05	0.38 (0.08 – 1.82)	0.23
< 50 years	13 (46.4)	1		1	
Monthly income					
< 170 USD	16 (36.4)	0.76 (0.30 – 2.01)	0.58	/	/
≥ 170 USD	12 (42.9)	1			
Sex					
Female	12 (40.0)	1.08 (0.42 – 2.83)	0.87	/	/
Male	16 (38.1)	1			
BMI					
<23 kg/m2	9 (52.9)	2.13 (0.70 – 6.42)	0.17	/	/
≥ 23 kg/m2	19 (34.5)	1			
Serum albumin					
< 35 g/l	11 (61.1)	3.42 (1.13 – 10.36)	0.02	0.66 (0.10 – 4.31)	0.67
≥ 35 g/l	17 (31.5)	1			
CRP					
≥ 6 mg/l	16 (59.3)	4.00 (1.45 –11.01)	0.006	3.80 (0.82– 17.71)	0.08
< 6 mg/l	12 (26.7)	1		1	
Bicarbonate					
< 22 mmol/l	9 (64.3)	3.69 (1.08 – 12.55)	0.0298	0.54 (0.08 – 3.50)	0.52
≥ 22 mmol/l	19 (32.8)	1		1	
Hemoglobin					
<10 g/dl	17 (56.7)	4.79 (1.50 – 15.23)	0.006	0.77 (0.16 – 3.78)	0.74
≥ 10 g/dl	6 (21.4)	1		1	
Protein intake					
< 0.8 g/kg/j	14 (63.6)	4.5 (1.55 – 13.06)	0.004	0.37 (0.07– 2.08)	0.26
≥ 0.8 g/kg/j	14 (28.0)	1		1	
eGFR					
<15 ml/min/1.73m2	21 (70.0)	11.67 (3.78 – 35.98)	<0.001	12.07 (2.49 – 58.55)	0.002
≥ 15 ml/min/1.73m2	7 (16.7)	1		1	
Total cholesterol					
≥ 2g/l	7 (35.0)	0.79 (0.27 – 2.32)	0.67	/	/
< 2g/l	21 (40.4)	1			

Abbreviations: eGFR, estimated Glomerular Filtration Rate; CRP, C-Reactive Protein; BMI, Body Mass Index

Predictive factors of malnutrition in patients with chronic kidney disease stages 3- 5 ND

Anemia (OR = 4.79; p = 0.006), low protein intake (OR = 4.5; p = 0.004), low serum albumin (OR = 3.42; p = 0.02), inflammation (OR = 4; p = 0.006), eGFR <15 ml/min (OR = 11.67; p < 0.001), and acidosis (OR = 3.69; p = 0.03) were associated with malnutrition however, on multivariate analysis, only a low eGFR<15 ml/min (OR = 12.07; p = 0.002) was predictive of malnutrition **(Table IV)**. Neither anthropometric nor bioimpedance indices were predictive of malnutrition **(Table III)**.

DISCUSSION

Studies on the nutritional status of non-dialyzed CKD populations in sub-Saharan Africa are sparse and none to the best of our knowledge in the CKD population in Cameroon. We have shown that 38.9% of non-dialyzed CKD patients in Cameroon are malnourished and that malnutrition increases with the severity of CKD; and that only a low eGFR<15ml/min is predictive of malnutrition in this population.

We observed an overall high prevalence of malnutrition at 38.9% in this study population, which is above the general country prevalence of 21% [7], suggesting a higher susceptibility of patients with CKD to malnutrition as has been reported elsewhere [2,8–13] . The frequency of malnutrition is however higher than reported rates in similar CKD populations in high income countries which vary from 19.6% in Australia [14] to 29% in Italy and the UK [15,16]. Low socioeconomic status, late presentation for nephrology care, and the lack of dietary interventions even in those who present early may explain the higher rates. Fifty percent in CKD stage 5 were on their first nephrology visit in the present study which is in consonance with previous reports from the same study setting. Late presentation for care in CKD precludes management of uremic complications and dietary interventions which may prevent malnutrition [14,15,17,18]. Diagnostic delays caused by various factors as well as weak health systems and policies in most of sub-Saharan Africa may account for the high frequency of late presentations [19,20]. The challenges in providing nutritional support to patients with CKD in Cameroon have been previously highlighted [21]. Only about 15% of the patients were on a CKD specific diet prescribed by a nephrologist. The lack of renal dieticians in the study setting has been previously reported [19,21]. Late presentation for nephrology care in CKD populations is well documented in low income countries including Cameroon which may be explained not only by lack of funds but weak healthcare systems and patient attitudes [19,22,23].

The prevalence of malnutrition increased with severity of CKD as has been reported elsewhere but the 70% prevalence in stage 5 observed in this study is much higher than the 40% reported at initiation of dialysis in Sweden [2]. This probably reflects the late presentation with no prior appropriate care observed in this study. Late presentation for nephrology care precludes adequate nutritional and other interventions to reduce malnutrition.

We found low protein intake (≤0.8g/kg/day), metabolic acidosis, inflammation, anemia, low serum albumin and low eGFR to be associated with malnutrition, however on multiple regression model, only eGFR <15 ml / min (OR = 9.80; p = 0.009) was an independent predictor of malnutrition. A low eGFR <15 ml / min has previously been reported as a predictor of malnutrition [15,24,25]. Indeed, the anorexia, severe metabolic acidosis, vomiting and hormonal abnormalities in end stage of kidney failure, a may lead to malnutrition.

Contrary to previous studies [8,13,15,24], we did not observe low protein intake, metabolic acidosis, inflammation, anemia, and low serum albumin as independent predictors of malnutrition in the present study probably due to the small sample size. There is however a strong relationship between malnutrition, inflammation, and atherosclerosis in CKD, whereby atherosclerosis is mediated by inflammation, malnutrition, oxidative stress, and genetic components [26,27]. This complex which involves inflammation and low serum albumin is considered a part of emerging non-traditional cardiovascular risk factors in CKD [28,29].

Anthropometric parameters were not predictors of malnutrition in this patient population. Previous studies have reported similar findings [8,15]. Indeed, the metabolic and hydro-electrolyte disorders caused by renal failure lead to a loss of muscle mass or, on the contrary, weight gain linked to fluid retention (which itself can be influenced by the treatment of renal failure). This makes anthropometric parameters a poor tool for assessing the nutritional status of patients with renal failure.

Bioimpedance parameters were not predictive of malnutrition, similar to the results of the Cupisti study [15]. However other studies have shown bioelectrical parameters to predict malnutrition when isotopic techniques based on total body potassium are used to assess body composition [14,30]. Standard bioelectrical impedance methods have previously been shown to be less reliable for point analysis of nutritional status in CKD especially in the presence of fluid overload [31].

Our study had several limitations: the small sample size, the semi-quantitative assessment of proteinuria, and the non-evaluation of adherence to diet. However, this pilot study shows a prevalence of malnutrition in patients with chronic renal failure. These findings highlight the importance of nutritional assessment and intervention in the care of non-dialyzed CKD populations especially those with anorexia and stage 5 CKD.

CONCLUSION

There is a high prevalence of malnutrition in the non-dialyzed CKD population in Cameroon, which increases with the worsening renal function. An eGFR<15 ml/min is an independent predictor of malnutrition. Neither anthropometric nor bio-impedance markers of nutritional status were predictive of malnutrition in this study.

Authors' contributions

Conception and study design: NAW, AG, NTG. Data collection: NAW. Data analysis and interpretation: NAW, AG. Manuscript drafting: NAW. Manuscript revision: NAW, AG, MM, NTG, KFF and NNEC. Guarantor of the study: AG. All the authors have read and agreed to the final manuscript.

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Conflicts of interest

The authors declare no conflicts of interest.

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Data sharing statement

No additional data are available.

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