Original paper

Determinants of Functional Status in End Stage Kidney Disease Patients on Maintenance Haemodialysis at Kenyatta National Hospital, Nairobi, Kenya

Suleh AA, Kayima JK, Kwasa JK

Department of Clinical Medicine and Therapeutics, School of Medicine, Faculty of Health Sciences, University of Nairobi, P.O. Box 19676-00202, Nairobi, Kenya

Address for Correspondence: Dr Audrey A Suleh. Email: audreynll91@gmail.com

Abstract

Background: Functional status refers to an individual's ability to conduct activities of daily living and includes functions such as feeding oneself, maintaining personal hygiene and transferring. Maintenance haemodialysis in End Stage Kidney Disease (ESKD) patients is linked to a significant decline in functional status and this decline is an important prognostic factor affecting the outcomes of this group of patients.
Objectives: The primary objective was to establish the functional status of ESKD patients on maintenance haemodialysis at the Kenyatta National Hospital (KNH) Renal Unit and grade it using the Karnofsky Performance Status scale. The secondary objective was to determine the selected factors associated with better physical function among ESKD patients on maintenance haemodialysis.
Methods: This was a cross-sectional descriptive study in which 82 patients with ESKD undergoing maintenance haemodialysis (>3 months) at the KNH Renal Unit were recruited. Relevant sociodemographic and clinical data was collected, and the Karnofsky Performance Status (KPS) scale was used to assess the functional status of the participants. The SPSS version 25 software was used for data entry and to perform the analyses. The participants' sociodemographic and clinical characteristics were summarized into percentages, means, standard deviations and median. Functional status was assessed using the KPS scale and categorized into either functionally dependent or independent and summarized as a percentage. A chi-square test of association and logistic regression was used to evaluate the relationship between functional status and the selected variables.
Results: The participants enrolled in the study were 82 with the median age being 46 years (inter-quartile range 34-58 years). Functional status was assessed with 44 (53.7%) participants being categorized as independent (KPS score 80-100%) and 38 (46.3%) being functionally dependent (KPS score <80%). In the univariable logistic regression model, age, dialysis vintage and fluid overload were significant predictors of functional status. The multivariable model demonstrated that dialysis vintage was a significant predictor at a 5% significance level.
Conclusion: Patients with ESKD undergoing haemodialysis at the KNH Renal Unit have a high prevalence of functional status impairment at 46.3%. Younger age, longer dialysis vintage and normal fluid status were the significant predictors of better physical function.

Key words: Functional status, Maintenance haemodialysis, End Stage Kidney Disease (ESKD)

Introduction

Patients diagnosed with chronic illnesses such as Chronic Kidney Disease (CKD) suffer from a considerable burden of functional status impairment (1). Functional status refers to the ability to conduct normal daily functions such as eating and grooming oneself that are necessary to meet basic needs and maintain well-being. One of the primary goals in healthcare is to maximize function in daily life (2) and for this reason, knowledge of the functional status is essential in prognostication of patients with CKD.

A change in the functional status is often the initial or only sign of development of an illness or worsening of any chronic disease. To achieve optimal health and well-being, it is important to understand the effect that diseases have on an individual's capacity to perform daily activities (3). There are several functional status assessment instruments available, and they include: The Karnofsky Performance Status (KPS) scale, the Katz Index of independence in activities of daily living (Katz ADL), Functional Index Measure (FIM), Barthel Index, Lawton Instrumental Activities of Daily Living (IADL) scale, the Functional Status Questionnaire,

among others. These functional status questionnaires include domains such as health, physical function, psychological and social function (4).

The high burden of functional status decline in patients undergoing maintenance haemodialysis may be attributed to several factors such as older age, comorbidities, frequent hospitalization, among others. Poor functional status impairs the well-being of patients and results in increased morbidity and mortality as demonstrated in previous studies done (1,5). Ifudu *et al* (6) demonstrated a high prevalence of functional dependence of 36% in dialysis patients in eight dialysis units located in urban New York and suburban New Jersey. The study concluded that the risk of having a poor functional status increased with presence of diabetes, female gender, Hispanic ethnicity, advanced age, and low serum creatinine concentrations.

In the Japan Dialysis Outcomes and Practice Patterns Study Phase V (J-DOPPS), functional status evaluation was done using the Katz index and Lawton Brody Instrumental Activities of Daily Living Scale (IADL scale) (1). Functional status decline was seen in 19.9% of the participants and had a significant association with increased mortality. Reduced functional status had a strong association with poor prognosis of patients undergoing haemodialysis and this was independent of demographic factors, laboratory values and comorbid conditions.

Studies done on functional status in the haemodialysis population in Africa are limited, however, in a study done in Kinshasa by Mokoli *et al* (7), 37.8% of patients had moderate to maximum physical incapacity. The factors that were independent predictors of lower physical incapacity included, a higher level of residual diuresis within 3 months of haemodialysis (P=0.024), absence of diabetes mellitus (P=0.024), good control of systolic blood pressure (P=0.013) and diastolic blood pressure (P=0.003) and erythropoietin use (P=0.004).

More recently in Cameroon, Mambap *et al* (8) also demonstrated an increase in the prevalence of functional decline in haemodialysis patients at 78.3% which is higher than in studies in New York, Japan, and Kinshasa. They found that the independent predictors of impaired functional status included a high daily pill-burden (p=0.043) and anaemia (p<0.001).

It is known that maintenance haemodialysis patients have a reduction in their functional status (9), however, there is limited data on the factors that contribute to this decline since functional status assessment is not done routinely in this group of patients. Incorporating functional status assessment in the management of these patients may help bridge this knowledge gap and help mitigate functional limitations and disability.

Materials and Methods

Study design: This was a descriptive cross-sectional study carried out at the Kenyatta National Hospital (KNH) Renal Unit.

Study population: The patients who were recruited into the study were any consenting individual above 18 years of age with End-Stage Kidney Disease (estimated Glomerular Filtration Rate (eGFR) of <15 mL/min) and had been on maintenance haemodialysis for a period of ≥3 months. Patients were excluded if they had acute illness in the last one month that may result in impaired physical function e.g., infection (pneumonia, sepsis), acute decompensated heart failure, pulmonary oedema.

Sample size: A target sample size of 82 was calculated using the Yamane's formula. Consecutive sampling was done until the required sample size was achieved.

Study procedures: Sociodemographic characteristics were collected using a researcher designed proforma. Functional status assessment was conducted by the principal investigator and the research assistant using the Karnofsky Performance Status (KPS) scale. The instrument has scores that range from 0 to 100 and higher scores signify a better functional status. In severe illnesses, the lower the score the poorer the prognosis. When the score is between 80 to 100, it indicates that the patient is functionally independent while a score <80 indicates that the patient is functionally dependent. (A score of 50 to 79 signifies that the patient is capable of self-care however requires assistance while <50 indicates that the patient is fully dependent).

Study variables: The dependent variable was the functional status. The independent variables were presence of comorbidities; age, nutritional status, haemoglobin level, fluid status, dialysis vintage and average Blood Urea Nitrogen (BUN).

Ethical considerations: Ethical approval was obtained from the University of Nairobi and Kenyatta National Hospital Ethical Research Committee prior to conducting the study. The ethical approval reference number for this study is P622/07/2022.

Data analysis: Statistical analysis was performed using the SPSS Version 25 Software. The baseline characteristics were reported using summary statistics such as the mean, median, standard deviation, and frequencies. Categorical variables were reported in the form of percentages and frequencies while the continuous variables were summarized as mean, median and standard deviation.

Functional status was categorized into either dependent or independent and reported as percentages. Based on the Karnofsky scale, a score of <80% is classified as dependent functional status while a score of 80 to 100% is classified as independent. The relationship between functional status and the selected variables was determined using a chi-square test of association and logistic regression.All statistical analyses were conducted at a 5% level of significance and a p value of < 0.05 was considered significant.

Results

The number of patients attending haemodialysis at the KNH Renal Unit who were screened was 92 but only 82 of them met the inclusion criteria and were included in the study.

Baseline characteristics: The median age of the participants was 46 years (interquartile range 34.3-59.3), 53.7% of the patients were males, 64.6% were unemployed, 41.5% had attained secondary level education, 93.9% had comorbidities where, 93.5% had hypertension and 36.4% had diabetes. Most of the patients (53.7%) had a short dialysis vintage of 3-6 months and 87.8% reported a dialysis frequency of two times per week (Table1).

Table 1: Baseline characteristics

Variable		Frequency N=82 Median (IQR)	(%)
Age (years)		46 (34.3-59.3)	
Sex	Male	44	53.7
	Female	38	46.3
Marital status	Married	56	68.3
	Single	20	24.4
	Separated / Divorced	6	7.3
Occupation	Actively employed	29	35.4
	Unemployed / retired	53	64.6
Level of education	Primary school	22	26.8
	Secondary school	34	41.5
	College	13	15.9
	University	10	12.2
	No formal education	3	3.7
Comorbidities	Yes	77	93.9
	No	5	6.1
Specification for comorbidities (n=77)	Diabetes	28	36.4
	Hypertension	72	93.5
	Cardiovascular diseases (IHD/DCM)	3	3.9
	Respiratory disease (Asthma/COPD)	6	7.8
	Stroke	3	3.9
	Hepatitis B	4	5.2
	Venous thromboembolism (DVT)	1	1.3
Dialysis vintage	3-6 months	44	53.7
	>6-12 months	11	13.4
	1-5 years	25	30.5
	>5 years	2	2.4
Frequency of dialysis	One time per week	8	9.8
	Two times per week	72	87.8
	Three times per week	2	2.4

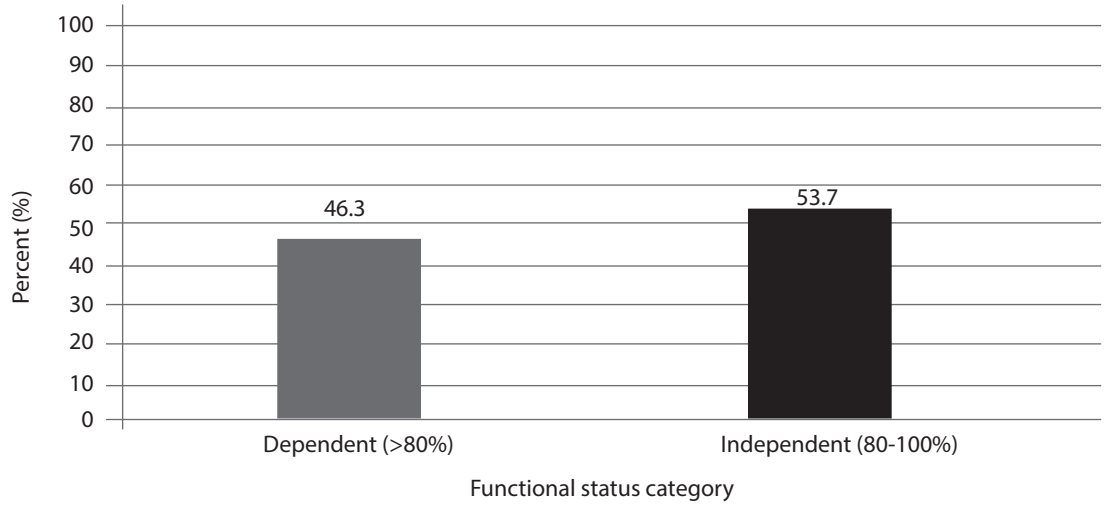
Baseline physical and laboratory characteristics: Most of the patients (57.3%) had a normal BMI (18.5-<25), 77.3% of the male and 55.3% of the female patients had a normal mid-upper arm circumference. More than three quarters of the patients (75.6%) had anaemia of ≤10g/dl and 58.5% had a BUN ≤20mmol/l. Over a third of the patients (46.3%) had fluid overload and 53.7% had a normal fluid status as shown in Table 2.

Table 2: Physical and laboratory characteristics

Variable		Frequency Median (IQR)	(%)
Nutritional status			
Weight (Kg)		63 (56.5-73)	
Height (cm)		162.5 (157-170)	
BMI (Kg/m^2)	Obese	8	9.8
	Overweight	19	23.2
	Normal	47	57.3
	Underweight	8	9.8
Mid-upper arm circumference (male)	≥23-29 cm (normal)	34	77.3
	<23 cm (malnourished)	6	13.6
	>29 cm (overweight)	1	2.3
	>30 cm (obese)	3	6.8
Mid- upper arm circumference (female)	≥22-28 cm (normal)	21	55.3
	<22 cm (malnourished)	9	23.7
	>28 cm (overweight)	2	5.3
	>29 cm (obese)	6	15.8
Lab tests			
Haemoglobin level	≤10g/dl	62	75.6
	>10g/dl	20	24.4
Pre-dialysis BUN	≤20mmol/l	48	58.5
	>20mmol/l	34	41.5
Fluid status			
Fluid status	Normal	44	53.7
	Fluid overload	38	46.3

Functional status using the Karnofsky Performance Status Scale: More than a half of the patients (53.7%, n=44) had independent functional status and 46.3% (n=38) had dependent functional status.

Figure 1: Functional status of ESKD patients on maintenance haemodialysis at KNH Renal Unit



Selected physical and laboratory characteristics associated with better physical function among ESKD patients on maintenance haemodialysis: The univariable analysis demonstrates that the variables: age <40 years (p=0.02), dialysis vintage of >1 year (=<0.001), and a normal fluid status (p=0.02) were significant predictors of better physical function among ESKD patients on maintenance haemodialysis (Table 3). The patients aged 40 years and above had 0.33 times lower odds of independence compared to those aged 18 to 39 years. Patients who reported a dialysis vintage of >1 year had 9.31 times higher odds of independence in comparison to those whose dialysis vintage was <1 year. Patients who had fluid overload had 0.34 times higher odds of functional impairment compared to those with a normal fluid status.

Table 3: Univariable logistic regression of functional status and selected physical and laboratory characteristics.

		Independent functional status	
Variable	n (%)	Odds ratio	P-value
Age (years)	(95% CI)		
40 and above	49 (59.8%)	0.33 (0.12-0.81)	0.02
Below 40	33 (40.2%)	Ref	Ref
Presence of comorbidities			
Yes	77 (93.9%)	0.27 (0.01-1.93)	0.25
No	5 (6.1%)	Ref	Ref
Dialysis vintage			
One year and above	27 (32.9%)	9.31 (3.08-35.19)	<.001
Below one year	55 (67.1)	Ref	Ref
Frequency of dialysis (per week)			
One time	8 (9.8%)	0	0.99
Two times	72 (87.8%)	0	0.99
Three times	2 (2.4%)	Ref	Ref
BMI			
Obese	8 (9.8%)	0.83 (0.14-1.80)	0.82
Normal	47 (57.3%)	2.03 (0.69-6.15)	0.20
Underweight	8 (9.8%)	2.29 (0.43-14.01)	0.34
Overweight	19 (23.2%)	Ref	Ref
MUAC			
Malnourished	15 (18.3%)	0.97 (0.40-2.36)	0.94
Normal		Ref	Ref
Haemoglobin level			
≤10g/dl	62 (75.6%)	1.58 (0.58-4.46)	0.37
>10g/dl	20 (24.4%)	Ref	Ref
Average BUN			
> 20mmol/L	34 (41.5%)	1.54 (0.63-3.81)	0.35
≤20mmol/L	48 (58.5%)	Ref	Ref
Fluid status			
Fluid overload	38 (46.3%)	0.34 (0.13-0.82)	0.02
Normal	44 (53.7%)	Ref	Ref

Table 4: Multivariable analysis of factors that predict better functional status (independent functional status)

Variable	Odds Ratio (95% CI)	P-value
Age (years)		
40 and above	0.42 (0.20-3.44)	0.11
Below 40	Ref	
Dialysis vintage		
One year and above	8.29 (2.58-33.00)	<0.001
Below oneyear	Ref	
Fluid status		
Fluid overload	0.80 (0.21-2.93)	0.73
Normal	Ref	
Intercept		0.78

In the univariable logistic regression, age, dialysis vintage and fluid status were the significant predictors of functional status. These independent variables were then subjected to the multivariable analysis (Table 4) and a dialysis vintage of >1 year was the only significant predictor (p=<0.001) of better functional status. The overall model however was not significant with a p-value of 0.78 (p>0.05) hence the univariable analysis findings were adopted.

Discussion

This study demonstrates that patients with ESKD undergoing maintenance haemodialysis at the KNH Renal Unit suffer from a considerable burden of functional status impairment. The Karnofsky Performance Status scale was utilized in assessing the physical function of patients on maintenance haemodialysis. Most of the respondents had full independence in performing ADLs with 44 (53.7%) patients scoring ≥80 on the KPS scale. Despite majority being able to perform ADLs independently, a considerable proportion i.e., 38 (46.3%) of the respondents had a low functional status score (KPS < 80) requiring assistance to carry out ADLs.

The high prevalence of functional status impairment has also been demonstrated in similar studies in other countries e.g., 19.9% in Japan (J-DOPPS study) (1), 36% in New York and sub-urban New Jersey (10), 37.8% in Kinshasa (7) and the highest prevalence of 78.3% in Cameroon (8). This demonstrates that patients with ESKD on haemodialysis suffer from functional impairment with a higher prevalence documented in developing countries in Africa. The risk of ESKD is greater in the African population compared to other races such as whites and a higher prevalence of morbidity because of complications related to ESKD (11). This may be one of the reasons for the higher prevalence of functional impairment noted in the African countries.

The presence of CKD imposes restriction in physical function. However, there are several factors that are known to contribute to a decline in functional status of patients on haemodialysis including presence of comorbidities and age, among others. In this study it was found that variables such as younger age (<40 years), dialysis vintage of >1 year and normal fluid status significantly predicted better physical function.

Age is one of the factors that predicts functional dependence in patients with ESKD undergoing haemodialysis. Older age is linked to a high level of disability and more frequent hospitalization, longer hospital stays and increased morbidity and mortality (11,12). The respondents in this study however, had a median age of 46 years which is similar to a study in Cameroon where the median age of the participants was 46.9±15 years (16). A higher median age was documented in Kinshasa 53 ± 11 years (15) and New York and sub-urban New Jersey 56± 14 years (14) but was highest in Japan (the J-DOPPS study) at 62.3 years (1). Like findings of previous studies (1,6,13,14) done on functional status of dialysis patients, this study also demonstrates a positive correlation between older age and decline in functional status (p=0.02). Cook *et al* (15) also demonstrated a high prevalence of impaired functional status of 75% among elderly patients on haemodialysis.

A longer dialysis vintage is usually linked to unfavourable outcomes and increased dialysis related complications (16). Among the respondents, a greater proportion of 44 (53.7%) had a shorter dialysis vintage of 3 to 6 months, 25 (30.5%) had a dialysis vintage of 1-5 years while 11(13.4%) respondents had a vintage of 6-12 months. However, in this study those with a longer dialysis vintage were noted to have better physical function (p<0.001). This is contrary to a study by Chertow *et al* (17)which concluded that a longer dialysis vintage resulted in a deterioration in nutritional parameters and a 6% increase in death. The patients recruited in the study by Chertow *et al* (17) had more frequent haemodialysis sessions of

three sessions per week compared to this study. In the current study most of the patients had two sessions of haemodialysis (87.8%) while only 2.4% attend thrice weekly haemodialysis and this may have contributed to less dialysis related complications that may impact functional status.

Fluid overload is one of the complications encountered in patients undergoing haemodialysis that impedes physical function and leads to frequent hospitalization and increased mortality. Methods used to assess fluid status such as bioimpedance spectroscopy, measurement of serum biomarkers like BNP are not readily available in public hospitals in our setting. In this study, fluid status was assessed clinically by measuring the jugular venous pressure and evaluating the patient for presence of peripheral oedema. The presence of an elevated jugular venous pressure and peripheral oedema is a sign of fluid overload in dialysis patients. There were 38 (46.3%) patients who had an elevated JVP (>4cm above the sternal angle). The odds of independence in performing ADLs were 2.96 times higher (p=0.02) in patients with a normal fluid status in comparison to those with fluid overload. This correlates with other studies that demonstrated that fluid overload contributes to impairment in physical function (18).

Anaemia in CKD patients is a factor that contributes to physical function impairment as demonstrated in previous studies such as the EURO-DOPPS (19). In the Canadian Erythropoietin Study Group Trial (20), administration of Epoetin-α in anaemic patients undergoing haemodialysis led to an improvement in exercise tolerance and physical function at month 2 and maintained through the 4th and 6th months. In this study, there was a high prevalence of anaemia with 62 (75.6%) participants having a haemoglobin level <10g/dl. However, contrary to other studies anaemia was not a significant predictor of functional status in this study. More studies in our setting involving larger sample sizes may be useful to assess the causal association between anaemia and functional impairment.

Patients with ESKD suffer from several comorbidities including cardiovascular diseases, diabetes mellitus, among others. The most common comorbidity in this study population was hypertension and was present in 72 (93.5%) patients, followed by diabetes in 28 (36.4%). The other less common diseases were stroke, respiratory diseases (asthma, COPD), hepatitis B and DVT. It is expected that presence of comorbidities impairs physical function however, no significant association was demonstrated between the presence of comorbidities and physical function in this study (p=0.25).

Uraemia has been linked to poor physical function. Uraemic myopathy is associated with decrease muscle oxygen utilization, and this leads to functional impairment in dialysis patients (21). In this study 34 (41.5%) of the participants had urea >20 while 45 (54.9%) had urea of ≤ 20mmol/l however, with no significant association demonstrated between elevated urea and functional status (p=0.35). Wyngaert *et al* (22) also demonstrated that there was a low association between functional measures of muscle strength and presence of uraemia. They attributed the high prevalence of functional impairment to other factors like presence of comorbidities and nutritional status.

Nutritional deficits and Protein Energy Wasting (PEW) are frequent complications affecting haemodialysis patients which result in negative outcomes and increased mortality. In this study we assessed nutritional status using BMI calculation and measurement of the MUAC. Most of the patients had a normal BMI accounting for 47 (57.3%) patients) while 8 (9.8%) patients were underweight. On assessment of the MUAC, we still had majority of the patients having a normal MUAC (31 males, 21 females) while 6 (13.6%) males and 9 (23.7%) females had a low MUAC (underweight). There was no positive correlation between low BMI and low MUAC and functional status (p=0.34). Lægrid *et al* (23) demonstrated a low BMI in older patients on dialysis, due to reduced food intake and unintentional weight loss although there was no significant association between nutritional status and physical function. Despite BMI being negatively correlated with physical function, malnutrition in dialysis patients is still worth evaluating during treatment. The AVANTE-HEMO Study (24) demonstrated that combining exercise and oral nutritional supplementation had a greater effect on improvement of physical function compared to oral nutritional supplementation alone.

Conclusion

There is a high prevalence of impairment in functional status at 46.3% in ESKD patients undergoing maintenance haemodialysis at the KNH Renal Unit. The factors that were found to be predictors of better physical function in this study were age <40 years (p=0.02), a longer dialysis vintage of >1 year (p<0.001) and a normal fluid status (p=0.02).

Recommendations

(i) It would be essential to perform functional status assessment for all patients who are being initiated on dialysis. This will guide in identifying and monitoring functional deficiencies over time and guide necessary interventions such as functional rehabilitation.

(ii) There is need for longitudinal studies to demonstrate how interventions such as nutritional supplementation, erythropoietin administration, physiotherapy or regular exercise programs impact survival outcomes in patients undergoing haemodialysis.

References

1. Matsuzawa R, Kamitani T, Roshanravan B, Fukuma S, Joki N, Fukagawa M. Decline in the functional status and mortality in patients on hemodialysis: Results from the Japan Dialysis Outcome and Practice Patterns Study. *J Renal Nutrition*. 2019; **29**(6):504–510.
2. Stewart AL, Greenfield S, Hays RD, Wells K, Rogers WH, Berry SD, *et al*. Functional status and well-being of patients with chronic conditions: Results from the medical outcomes study. *J Amer Med Ass*. 1989; **262**(7):907–913.
3. Kavanagh NT, Schiller B, Saxena AB, Thomas IC, Kurella Tamura M. Prevalence and correlates of functional dependence among maintenance dialysis patients. *Hemod Intern*. 2015; **19**(4):593–600.
4. Doble OCCU S, Fisher T. Assessing function in the elderly: Katz ADL and Lawton IADL. 2008.
5. Kurella Tamura M, Covinsky KE, Chertow GM, Yaffe K, Seth Landefeld C, McCulloch CE. Functional status of elderly adults before and after initiation of dialysis. *N Engl J Med*. 2009; **361**(16):1539-47.
6. Ifudu O, Paul HR, Homel P, Friedman EA. Predictive value of functional status for mortality in patients on maintenance hemodialysis. *Clinical study. Am J Nephrol*. 1998; **18**: (2):109-116
7. Mokoli VM, Bukabau JB, Izeidi PPO, Luse JL, Mukendi SK, Mashinda DK, *et al*. Prédicteurs du degréd'incapacité physique chez les hémodialysés de Kinshasa: rôle primordial de la diurèserésiduelle. *Nephrologieet Therapeutique*. 2016; **12**(7):530–535.
8. Mambap AT, Che IA, Mahamat M, Ashuntantang GE. Functional status and caregiver burden of patients on maintenance haemodialysis in Cameroon: a two-centre cross-sectional study. *BMC Nephrol*. 2022; **23**(1):
9. Avesani CM, Trolonge S, Deléaval P, Baria F, Mafra D, Faxén-Irving G, *et al*. Physical activity and energy expenditure in haemodialysis patients: An international survey. *Nephrol Dialysis Transplant*. 2012; **27**: 2430–34.
10. Ifudu O, Paul H, Mayers JD, Cohen LS, Brezsnyak WF, Herman AI, *et al*. Pervasive failed rehabilitation in center-based maintenance hemodialysis patients. *Amer J Kidney Dis*. 1994; **23**(3):394–400.
11. Nzerue CM, Demissachew H, Kevin Tucker J, *et al*. Race and kidney disease: Role of social and environmental factors. *J Natl Med Assoc*. 2002; **94**(8 Suppl):28S-38S.
12. Shah S, Leonard AC, Thakar CV. Functional status, pre-dialysis health and clinical outcomes among elderly dialysis patients. *BMC Nephrol*. 2018; **19**(1): 100.
13. Stanisławska J, Talarska D, Niewiadomski T, *et al*. The functioning of patients on haemodialysis. Age as the main determinant of functional condition. *Med Res J*. 2020; **5**(4):231–237.
14. Lai YC, Wang CY, Moi SH, *et al*. Factors associated with functional performance among patients on hemodialysis in Taiwan. *Blood Purif*. 2018; **46**(1):12–18.
15. Cook WL, Jassal SV. Functional dependencies among the elderly on hemodialysis. *Kidney Int*. 2008; **73**(11):1289–95.
16. Sumida K, Yamagata K, Iseki K, *et al*. Different impact of hemodialysis vintage on cause-specific mortality in long-term hemodialysis patients. In: Nephrology Dialysis Transplantation. Oxford University Press; 2016. p. 298–305.
17. Chertow GM, Johansen KL, Lew N, *et al*. Vintage, nutritional status, and survival in hemodialysis patients. *Kidney Intern*. 2000; **57**(3):1176-81.
18. Hsiao SM, Tsai YC, Chen HM, *et al*. Association of fluid status and body composition with physical function in patients with chronic kidney disease. *PLoS One*. 2016; **11** (10): e0165400.
19. Locatelli F, Pisoni RL, Combe C, *et al*. Anaemia in haemodialysis patients of five European countries: Association with morbidity and mortality in the Dialysis Outcomes and Practice Patterns Study (DOPPS). *Nephrol Dialysis Transplant*. 2004; **19**(1):121–132.
20. Muirhead N, Keown PA, Churchill DN, *et al*. Dialysis patients treated with Epoetin α show improved exercise tolerance and physical function: A new analysis of the Canadian Erythropoietin Study Group trial. *Hemod Intern*. 2011; **15**(1):87–94.
21. Johansen KL. Physical functioning and exercise capacity in patients on dialysis. *Adv Ren Replace Ther*. 1999; **6**(2):141-148.
22. Wyngaert K Vanden, Van Craenenbroeck AH, Holvoet E, *et al*. Composite uremic load and physical performance in hemodialysis patients: A cross-sectional study. *Toxins* (Basel). 2020; **12**(2):
23. Lægreid IK, Aasarod K, Bye A, *et al*. The impact of nutritional status, physical function, comorbidity and early versus late start in dialysis on quality of life in older dialysis patients. *Ren Fail*. 2014; **36**(1):9–16.
24. Martin-Alemañy G, Espinosa-Cuevas M de los Á, Pérez-Navarro M, *et al*. Effect of oral nutritional supplementation with and without exercise on nutritional status and physical function of adult hemodialysis patients: A parallel controlled clinical trial (AVANTE-HEMO Study). *J Renal Nutrition*. 2020; **30**(2):126–136.