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Early Mortality (120 Days) amongst Incident Hemodialysis with End Stage Kidney Disease: A 5-Year Retrospective Study

Denis Georges Teuwafeu[1], Dianna Fontania Mafouk Fopa[1], Halle Marie Patrice[2], Ronald Gobina[1], Maimouna Mahamat[3], Hermine Fouda[3], Kaze Folefack Francois[3]

[1]Faculty of Health Sciences, University of Buea, Buea, Cameroon
[2]Faculty of Medicine and Pharmatical Sciences, University of Douala, Douala, Cameroon
[3]Faculty of Medicine and Biomedical Sciences, University of Yaoundé, Yaoundé, Cameroon
Email: d.teuwafeu@yahoo.com

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Abstract

Background: End stage kidney failure (ESKF) is a major public health problem worldwide. Haemodialysis is the principal method in its management, and is associated with high mortality mostly owing to cardiovascular disease (CVD). In Cameroon, data on its predictors is lacking. **Objectives:** This study aimed at determining the 120 day mortality, causes of death and its predictors and amongst incident haemodialysis patients with end stage kidney disease in Cameroon. **Methods:** We retrospectively reviewed medical records of patients admitted for ESKF who started haemodialysis between January 2016 and December 2020 (5 years) and who died within 120 days. For these patients, the variables collected were: age, gender, comorbidities, dialysis parameters, para-clinical parameters, cause of death. The causes of death were registered as stated by the attending physician. Data were analysed using SPSS 20. A p-value < 0.05 was considered significant. **Results**: Out of 1012 incident patients, 258 died giving a mortality rate of 25.5%. Of these, 59.7% were males. The mean age (SD) was 46.52 (15.6) years. The main causes of death included sepsis (45.61%), CVD (12.86%), and severe anaemia (9.94%); and were comparable between males and females except for anaemia which was more prevalent in females (p = 0.003). Catheters related infections (77.9%), and chest infections (9.0%) were the main sources of sepsis while sudden death (76.2%), myocardial infarction (9.5%), and heart failure (9.5%) were the main cardiovascular causes of death. Hypertension (65%), CVD (35.6%), and diabetes (9.19%) were the main comorbidities associated to death. The main vascular access was central venous catheter 96%. CVD (p = 0016, aOR; 4.107), Albumin ≤ 3.5 g/dl (p = 0.015, aOR; 23.083), and Creatinine > 20 mg/dl (p = 0.024, aOR; 5.649) were independent predictors of mortality. **Conclusion:** One in four patients on haemodialysis died early. CVD, hypoalbuminemia

and late initiation were predictors of mortality. Majority of patients die from preventable causes, with sepsis from catheter being the most frequent.

Keywords

Early Mortality, Predictors, Causes of Death, Haemodialysis, Cameroon

1. Background

Chronic kidney disease (CKD) is a non-communicable disease, and a major public health problem ranked as the 12th cause of death worldwide in 2017 [1]. Its final common pathway, End Stage Kidney Failure (ESKF), is associated with considerable morbidity and mortality [2] [3]. It is estimated that by 2030, 70% of patients with ESKF will originate from low- and middle income countries (LMICs), such as those in sub-Saharan Africa [4] [5]. This is driven by population aging, the double burden of infectious diseases and the growing problems of other non-communicable diseases such as obesity, diabetes mellitus and hypertension [6] [7] [8]. Once the kidneys fail, renal replacement therapy (RRT) is the only means of survival [9] [10]. Where available, haemodialysis predominates because of frequent unavailability and higher costs of peritoneal dialysis or transplantation [11] [12]. However, dialysis patient mortality is unacceptably high, currently approximately 20% per year in the United States [13]. The mortality rate within 90 days of commencing RRT in SSA countries is as high as 90%, compared with European countries where it is about 3% [4] [14]. Despite the technical advances in haemodialysis [13] [15], the mortality of patients with ESKF is 10 to 30 times higher than that of the general population [4]. In developing countries, the mortality is even higher due to the lack of human, financial and material resources [16]. The mortality among incident haemodialysis patients in Cameroon was reported to be 39% [8], with the most common causes of death being cardiovascular, infectious disease, uremic complications and anaemia [17] [18] [19]. Cardiovascular diseases are the leading [20] cause of death in ESKF patients; cardiac arrest accounts for 47.1% of total deaths [21] [22]. Knowing whether risk factors for mortality differ in dialysis patients who survive longer and the strengths of these risk factors for mortality change over time would assist physicians in making better prognostic judgments [23]. Few studies have performed a comprehensive analysis of the prognostic importance [2] of comorbidities, age, sex, nutritional status in incident dialysis patients' survival [24] [25] [26]. Cardiovascular disease and the timing of dialysis initiation have equally served as important prognostic markers of survival, independent of other factors [25] [27]. In our setting, data on the early mortality, the causes of death and its predictors is scarce, hence the interest of this work.

2. Patients and Methods

2.1. Study Setting

This was a retrospective study from in two haemodialysis units, government

funded and offering two dialysis sessions of 04 hours per week. These are the main referral centres for patients with kidney failure covering two regions of about four million population. Both hospitals serve as teaching hospital and referral hospital for their regions and the nation. The Douala general hospital is a tertiary hospital, and the dialysis centre has 25 dialysis machines, 2 nephrologists for a total of 250 patients. The Buea Regional hospital is a secondary hospital, his dialysis centre has 08 machine, 2 nephrologist and a total of 100 patients. In both hospitals, patient with kidney failure are screened in the emergency and referred to the nephrologist who is in charge of evaluating the severity of the disease, indication for dialysis, initiation on dialysis, admission, discharge and follow up of the patient. There is no universal health coverage and patient pay out of pockets for vascular access creation, laboratory tests and medications. The government only subsidised the dialysis treatment for which the patient contribution is 5000 XFA (10 US $) for each session.

2.2. Participant Selection

From the dialysis registries, we sorted out all incident patients admitted on dialysis for end stage renal failure, from 01st January 2016 to 31st December 2020. We included all incident HD patients with ESKF who died within the first 120 days of HD initiation.

2.3. Ethical Approval

Ethical approval was obtained from the Institutional Review Board of the Faculty of Health Sciences, University of Buea, and Ethics Committee No. 2584. Administrative authorisation was sought and obtained from the administration of both hospitals.

2.4. Data Collection and Management

The medical records of all patients who died within 120 days of haemodialysis initiation were included in this study. The date of death was collected as recorded in the death registries, or exploiting hospitalization files. Similarly, the cause of death was gotten by either exploiting the records of patients who died while in the hospital (cause of death as stated by the attending physician) or by exploiting the circumstances surrounding the last medical visit of the patient (clinical presentation, laboratory investigations, event in the last dialysis as well as duration between the last dialysis and the date of death). For these patients, baseline demographic data such as age, gender, residential details, marital status, and comorbidities such as diabetes, hypertension, cardiovascular disease, cerebrovascular accident, HIV, hepatitis B and malignancy were collected. The primary renal diagnosis was recorded as stated by the treating nephrologist at the time of dialysis initiation. Para-clinical investigations within one month of haemodialysis initiation were also recorded and included serum urea, creatinine, haemoglobin, potassium, phosphorus, calcium, C-reactive protein, serum albumin.

2.5. Definition of Operational Terms

Early mortality: mortality that occurred within 120 days of dialysis initiation.

End stage kidney failure (ESKF): any patient with a documented history of ESKF as diagnosed by a nephrologist.

Incident haemodialysis patients: incoming patients with ESKF who had their first dialysis session between 01st January 2016 and 31st December 2020.

Comorbidity: the presence of additional or co-existing diseases with reference to ESKF and its aetiology as the initial diagnosis.

Cardiovascular death: death from any cardiovascular mechanism like stroke, myocardial infarction, heart failure, arrhythmia, sudden death.

Catheter infection: temperature ≥ 38˚C in a patient having a catheter and/or presence of local signs of infection (inflammation, suppuration) with or without bacterial culture, with no other aetiology found.

Severe Anaemia: a haemoglobin level of 7 g/dl.

Uremic syndrome: occurrence of signs and symptoms of chronic uraemia with no other aetiology identified in a patient with ESKF.

2.6. Data Management and Analysis

Analyses were done using the statistical package software SPSS 20. Chi square and Fischer's exact statistical test were used to assess associations between variables. Categorical variables were summarized using counts and percentages. Continuous variables using means, standard deviations, medians and interquartile ranges where necessary. Logistic regression analysis was used to look for predictors. A p value < 0.05 was considered statistically significant.

3. Results

3.1. Mortality among Study Population

Out of 1012 Incident patients, 258 died within 120 days. The mortality rate was calculated at 25.5%. As shown in Table 1, mortality was highest during the first 30 days (46.5%), amount male (59.7%) and within the 45 - 65 years age group (46.0%). Central venous catheter was the principal (96%) vascular access at death. Non communicable diseases where the main comorbidities at death.

3.2. Causes of Death

Cause of death could be identified in 164 cases. The principal causes of death were sepsis (n = 78, 47.5%), cardiovascular disease (n = 21, 13.4%), and anaemia (n = 17, 10.3%) but one out of 4 patients (n = 39) died of complications of kidney failure (Figure 1). Causes of death were comparable between males and females except for anaemia which was more prevalent among females (p = 0.003). Cardiovascular disease was most common cause in the age group 16 - 45 years and accounted for 50%. Throughout the 120 days, catheters were the main causes of sepsis and the prevalence of catheter related sepsis increase gradually from 74% to 90% during the first three months and dropped to 70% during the fourth

Table 1. Characteristics of the participants.

Category		Frequency	Percentage
Gender	M	154	59.7%
	F	104	40.3%
Age Group (years)	<15	8	3.1%
	15 - 44	108	45.7%
	45 - 65	118	46.0%
	>65	24	9.3%
Duration in dialysis (days)	0 - 30	120	46.5%
	31 - 60	70	27.0%
	61 - 90	45	17.5%
	91 - 120	23	9.0%
Dialysis access at death	CVC	247	96%
	AVF	11	4%
Comorbidities at death	HTN	118	45.6%
	Cardiovascular diseases	62	24.1%
	Diabetes	19	7.5%
	Cerebrovascular diseases	12	4.8%
	HIV	10	4.0%
	Malignancy	10	4.0%
	Other*	27	10.0%

CVC: central venous catheter, FAV: arterio-venous Fistula HTN: hypertension HIV/AIDs: human immunodeficiency virus. *Hepatitis B and C virus = 10, multiple myeloma = 3, gout = 3, not specified = 11.

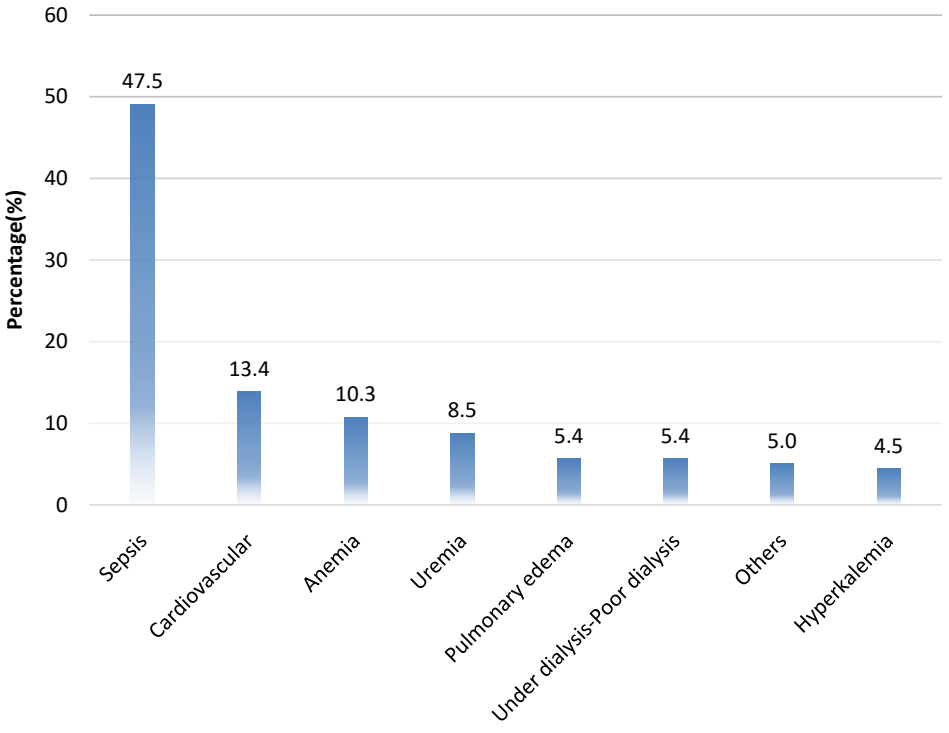

Figure 1. Principal causes of death. #: others; malignancy = 2, trauma = 1, liver failure = 1, pneumothorax = 1.

month. Other causes of sepsis included, Community acquired pneumonia, gastroenteritis, pyelonephritis (Figure 2). Among cardiovascular deaths, sudden death (n = 16, 76.2%), myocardial infarction (n = 2, 9.5%) and heart failure (n = 2, 9.5%) were the most frequent (Figure 3).

3.3. Predictors of Mortality

On bivariate analysis, mortality rate was higher in patients with CVD (OR: 6.9, p = 0.001), patients with catheter as first vascular access (OR: 7.0, p < 0.0001). Age, gender and the presence of diabetes did not show any association with death at 120 days (Table 2). Albumin level less than or equal to 3.5 g/dl (OR: 17, p = 0.001), CRP > 12 mg/l (OR: 3, p = 0.046), creatinine > 20 mg/dl (OR: 6.9, p = 0.001) and urea > 300 mg/dl (OR: 4.0, p = 0.049) were negatively associated with mortality (Table 3).

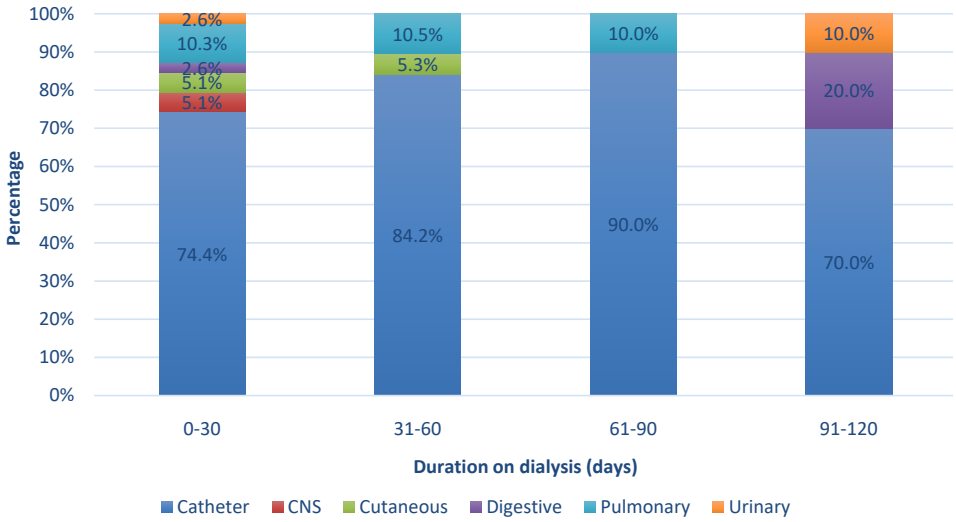

Figure 2. Origin of sepsis according to duration on dialysis. CNS: central nervous system.

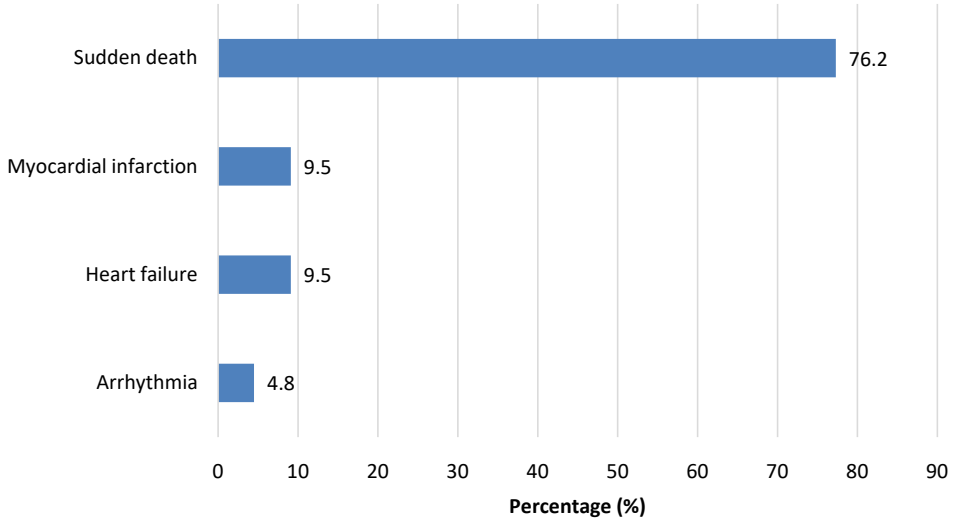

Figure 3. Cardiovascular causes of death.

Table 2. Socio-demographic and clinical characteristics associated to mortality (bivariate analysis).

Variable	category	Died (%)	Alive (%)	OR	CI 95%	p-value
Age (year)	<15	9 (3.4)	1 (1.1)	-	-	Ref
	16 - 65	226 (87.5)	93 (95.7)	0.188	0.06 - 3.71	0.116
	>65	23 (8.91)	3 (3.1)	0.452	0.08 - 9.30	0.452
Gender	Male	89 (59.7)	57 (57.5)	-	-	Ref
	Female	67 (40.3)	42 (42.4)	0.979	0.59 - 1.63	0.934
HTN	Yes	57 (65.5)	43 (79.6)	0.486	0.22 - 1.08	0.076
	No	30 (34.5)	11 (20.4)	-	-	Ref
Diabetes	Yes	8 (9.1)	2 (3.7)	2.633	0.54 - 12.89	0.232
	No	79 (90.8)	52 (96.3)	-	-	Ref
HIV	Yes	5 (5.74)	4 (7.4)	0.762	0. 20 - 2.97	0.696
	No	82 (94.2)	50 (92.6)	-	-	Ref
CVD	Yes	31 (35.6)	4 (7.4)	**6.920**	2. 28 - 20.97	**0.001****
	No	56 (64.4)	50 (92.5)	-	-	Ref
CVA	Yes	6 (6.9)	1 (1.8)	3.926	0. 46 - 33.54	0.211
	No	81 (93.1)	53 (98.2)	-	-	Ref
Vascular Access	Catheter	146 (96.1)	69 (77.5)	**7.053**	2.71 - 19.35	**<0.001****
	Fistula	6 (3.9)	20 (22.5)	-	-	Ref

OR, Odds Ratio; Ref, Reference, HTN, Hypertension; CVD, Cardiovascular disease; CVA, Cerebrovascular accident. ** means significant value.

After logistic regression, independent predictors of mortality were Cardiovascular disease (AOR: 4.107; 95% CI: 1.30 - 12.93; p = 0.016), albumin less than or equal to 3.5 g/dl (AOR: 23.083; 95% CI: 1.85 - 288.45; p = 0.015) and creatinine > 20 mg/dl (AOR: 5.649; 95% CI: 1.25 - 25.49; p = 0.024) at initiation (Table 4).

4. Discussion

The aim of this study was to determine the 120 day mortality rate, identify the causes of death and discuss its predictors among incident haemodialysis patients with ESKF at Douala General Hospital and Buea Regional Hospital from January 2016 to December 2020. At the end of the study; 1012 patients registered in these centres over the study period, 258 deaths were recorded within 120 days thus a rate of 25.5% (23, 1% at DGH and 28, 6% at BRH). The main causes of death were sepsis (47.5%), cardiovascular diseases (13.4%), and anaemia (10.3%). Sepsis among these patients originated principally from catheters (77.9%), and the lungs (9.0%). Cardiovascular deaths were mostly sudden deaths (76.2%), myocardial infarction (9.5%) and heart failure (9.5%). Older age, cardiovascular disease, having a catheter as first vascular access, Albumin ≤ 3.5 g/l, CRP > 12 mg/l,

Table 3. Paraclinical data associated with mortality.

Variable	Dead n (%)	Alive n (%)	OR	CI 95%	p value
Haemoglobin (g/dl)					
<7	30 (35.7)	17 (23.6)	**7.059**	0.73 - 68.37	0.092
7 - 10	53 (63.1)	51 (70.8)	**4.157**	0.50 - 38.46	0.209
>10	1 (1.2)	4 (5.6)	Ref	Ref	Ref
Albumin(g/dl)					
≤3.5	17 (81.0)	4 (19.0)	**17**	3.93 - 73.58	**<0.001****
>3.5	5 (20.0)	20 (80.0)	Ref	Ref	Ref
Potassium (mEq/L)					
>4.5	26 (49.1)	12 (41.4)	**2.167**	0.46 - 10.16	0.327
3.5 - 4.5	23 (43.4)	13 (44.8)	**1.769**	0.38 - 8.28	0.469
<3.5	4 (7.5)	4 (13.8)	Ref	Ref	Ref
CRP (mg/L)					
<12	8 (13.8)	10 (38.5)	Ref	Ref	Ref
12 - 96	39 (67.2)	16 (61.5)	**3.047**	1.022 - 9.12	**0.046****
>96	11 (19.0)	0 (00)	**-**	-	
Creatinine (mg/dl)					
>20	23 (29.9)	4 (6.2)	**6.948**	2.11 - 22.86	**0.001****
10 - 20	30 (39.0)	32 (49.2)	**1.133**	0.54 - 2.36	0.740
<10	24 (31.2)	29 (53.7)	Ref	Ref	Ref
Calcium (mg/dl)					
≤8.3	32 (65.3)	25 (46.3)	**2.184**	0.99 - 4.84	0.054
>8.3	17 (34.7)	29 (53.7)	Ref	Ref	Ref
Phosphorus (mg/dl)					
>5	17 (37.8)	17 (38.6)	0.786	0.28 - 2.22	0.649
4 - 5	14 (31.1)	16 (36.4)	0.668	0.24 - 2.00	0.491
<4	14 (31.1)	11 (25.0)	Ref	Ref	Ref
Urea (mg/dl)					
>300	11 (32.4)	7 (11.7)	**4.086**	1.01 - 16.58	**0.049****
100 - 300	18 (52.9)	40 (66.7)	**1.170**	0.36 - 3.78	0.793
<100	5 (14.7)	13 (21.7)	Ref	Ref	Ref

CRP, C-reactive protein. ** means significant value.

Table 4. Predictors of mortality (multivariate analysis).

Variable	Dead n (%)	Alive n (%)	AOR	95% CI	p value
CVD	31 (35.6)	4 (7.4)	**4.107**	1.30 - 12.93	**0.016****
Catheter	146 (96.1)	69 (77.5)	**-**	2.71 - 19.35	**.**
Albumin (g/dl)					
≤3.5	17 (81)	5 (20)	**23.083**	1.85 - 288.45	**0.015****
CRP (mg/l)					
12 - 96	39 (67.2)	16 (61.5)	**-**	**-**	**-**
Creatinine (mg/dl)					
>20	23 (29.9)	4 (6.2)	**5.649**	1.25 - 25.49	**0.024****
Urea (mg/dl)					
>300	11 (32.4)	7 (11.7)	**1.755**	0.34 - 8.94	0.498

AOR, Adjusted Odds Ratio, CVD, Cardiovascular disease, CRP, C-reactive protein. ** means significant value.

Creatinine > 20 mg/dl, and Urea > 300 mg/dl were associated with mortality. After multivariate analysis, cardiovascular disease, Albumin ≤ 3.5 g/l, and Creatinine > 20 mg/dl were independent predictors of mortality.

Early mortality among incident haemodialysis patients is still very high despite the technical and pharmacological advances in the field of medicine. We recorded a rate of 25.5%, which was similar to 27.5% reported by Ortiz *et al.* in the US in 2011 [20]. Halle *et al.* in 2013 recorded a higher mortality of 34%, Fouda *et al.* in 2005 had a 90 day mortality about twice that of our study [4] [16]. This drop in mortality could be explained by the fact that there has been an increase in the number of haemodialysis centres in the country passing from 3 to more than 8 centres. Our mortality rate was otherwise at least four times that recorded by Tsakiris *et al.*, Ansell *et al.* and Mcquillan *et al.* which were respectively 3.9%, 5.8% and 6.3% [28] [29] [30]. This great disparity could be explained by the fact that RRT in our setting albeit available is limited, there is insufficient pre-dialytic care as well as the cost associated with the management of ESKD, its comorbidities and complications [31] [32]. Luyckx *et al.* in 2013 quoted that; many people whose kidneys fail can expect to live long, but only if they live in rich countries [33].

Mortality was higher at the BRH compared to the DGH. This could be explained by the fact that the DGH is an older centre, and also as a tertiary hospital has a better technical plateau in terms of staff and material. This will definitely imply a better management of these patients, their comorbid conditions and complications. Also, more patients at the DGH are insured and this goes a great deal with the cost of care. In addition to this, a good number of patients at the BRH come from rural areas and access is not the best. With the ongoing socio-political crisis, there are also shortcomings with transportation and accessibility.

The principal cause of death was sepsis (n = 78; 47.5%), with catheter as the principal origin of sepsis (77.9%, n = 60) throughout this period. This is similar to other studies in developing countries where sepsis was reported as the first cause of death, this was the case in Ethiopia were sepsis accounted for 34.1% of causes of death, in Saudi Arabia where it was 45% [9] [34]. In these, catheters were yet the most common origin of sepsis. This high level of death due to sepsis could still be explained by the excessive use of temporal catheters at initiation of dialysis which is a risk factor for developing infections. Cardiovascular diseases represented the second causes of death (12.82%), as was equally reported in the same studies above [9] [34]. Sudden death (76.2%), myocardial infarction (9.5%) and heart failure (9.5%) were the main cardiovascular causes of death in our study. Even though in literature cardiovascular diseases are the main causes of death, it takes the second position in low income countries probably because of the burden of infectious diseases in these countries, lack of pre dialysis follow up as seen with the use of temporal catheters for dialysis and the poor management of complications associated with ESKF. This is however different from the studies done in developed countries, where cardiovascular death is still the leading

cause of death. This was the case in Canada (34.2%), South Korea (41.6%) [30] [35]. Among cardiovascular deaths, sudden death was the most frequent, a finding similarly reported in the above studies. This difference with high income countries could be explained by their population entering dialysis at an elderly age, above 65 years and presenting with numerous cardiovascular comorbidities, coupled with their quality of care [36]. Anaemia was the third cause of death, accounting for 9.94% and was more prevalent in females ($p = 0.003$). This could be explained by the cost of care with anaemia, notably: blood transfusions, the use of erythropoietin (EPO) and this poses a financial burden. Though we did not evaluate the impact of economic status due to the retrospective nature of our study, women are usually underprivileged and unemployment is more encountered amongst them. This was reported by Halle *et al.* in 2015 in one of these centres [37]. Uraemia accounted for 8.8% of deaths, which was less than that reported by Fouda *et al.* [16]. This could be explained by the fact that there were fewer haemodialysis centres during her study period and patient this could not accommodate the ESKF population in the country at the time.

We found that several factors were associated with mortality. These included; older age, having a catheter as first vascular access type, cardiovascular disease, Albumin ≤ 3.5 g/l, CRP > 12 mg/l, Creatinine > 20 mg/dl, and Urea > 300 mg/dl. After logistic regression, cardiovascular disease, Albumin ≤ 3.5 g/l, and Creatinine > 20 mg/dl were independent predictors of mortality. Cardiovascular disease has been reported as a predictor of mortality in a number of studies. This was reported by Bradbury *et al.* in 2007 in the Dialysis Outcomes and Practice Patterns Study and Mcquillan *et al.* in 2012 in Canada [13] [30]. In a study done by Tong *et al.* in 2015, CVD was associated with worse survival rates in dialysis patients [38], Foley *et al.* in 2012 reported CVD-related mortality in dialysis patients to be 10 to 20 times higher than in the general population [39]. Hypoalbuminemia (albumin ≤ 3.5 g/l) was associated with mortality. Inflammatory states, under nutrition amongst our population, could be responsible for this picture, as equally reported by Canaud *et al.* in 2013 [40]. It is very likely that much of the influence of nutritional biochemical parameters, particularly albumin, on the morbidity and mortality of dialysis is explained by the relationship between inflammation and this parameter [24] [41]. It has been reported that in the presence of chronic inflammation, malnourished patients have very low albumin levels, a sign of severity of malnutrition or a reflection of resistance to treatment [42]. Lukowsky *et al.* in 2012 showed that a higher creatinine at dialysis initiation was associated with mortality, similarly for higher urea levels [17]. The above association summarises the disconcerting high rate of late referral to nephrologists in our setting, with already worsened renal failure at HD initiation [37]. Similarly, an inverse relationship has been described between creatinine and mortality owing to sarcopenia/protein energy malnutrition [43] [44].

Limitations and Strength

We acknowledge some limitations to this study. The retrospective nature of our

study makes a lot of data missing. The mortality rate calculated above is probably just an underestimate as some patient deaths may not have been reported, and others lost to follow-up. The causes of death were based on clinical judgement and individual perception of the nephrologist or general practitioner during last admission or medical visit. Nonetheless, this was a multicentre study at different levels of care.

5. Conclusion

One in four patients on haemodialysis die early. Cardiovascular disease, hypoalbuminemia, and worsened renal failure were predictors of mortality. Majority of patients die from preventable causes, the main ones were sepsis from catheter, cardiovascular diseases, and severe anaemia.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Abbreviations

BRH: Buea Regional Hospital,
CKD: Chronic Kidney Disease,
CVD: Cardiovascular Disease,
DGH: Douala General Hospital,
ESKF: End Stage Kidney Failure,
HD: Haemodialysis,
HIV: Human Immunodeficiency Virus,
IHD: Incident Haemodialysis,
LMICs: Low and Middle Income Countries,
NCDs: Non-Communicable Diseases,
RRT: Renal Replacement Therapy,
SSA: Sub-Saharan Africa,
WHO: World Health Organisation.