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Intradialytic Hypertension and Associated Factors among Chronic Haemodialysed Patients in Sub-Saharan Africa: An Example from Cameroon

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Abstract

Background: Hemodialysis (HD) is a therapy during which complications such as intradialytic hypertension (IDH) are frequent. We aimed to determine the incidence of IDH and associated factors amongst patients on maintenance hemodialysis in Cameroon. **Method:** It was a prospective cohort study including end stage kidney disease patients on HD. Data collected were: socio-demographic, comorbidities, current medication, weight, heart rate ultrafiltration rate (UF), albuminemia and electrocardiogram. The first blood pressure (BP) measurement was obtained at the beginning of the session and the last at the end. IDH was defined as an increase in systolic BP ≥ 10 mmHg between the first and the last measurement. Logistic regression was used to look for associated factors, p-value < 0.05 was considered significant. **Results:** Mean age was 49.06 ± 13.97 years with 64.2% males. Mean number of dialysis session was 11.26 ± 2.49. Incidence of IDH was 48.36%. The median number of IDH episodes was 5 (Range 0 - 12). Factors increasing the risk were hypertension (p = 0.003), number of antihypertensive drugs ≥ 2 (p < 0.001), blood transfusion during the session (p < 0.001), male gender (p = 0.038) and a monthly income < 35000 XAF (p = 0.033). Factors lowering the risk were age ≥ 50 years (p = 0.012), longer duration on dialysis (p < 0.001), dry weight ≥ 67 kg (p < 0.001), UF ≥ 800 ml/h (p < 0.001) and a BP ≥ 140/90 mmHg at the beginning of the session (p < 0.001). **Conclusion:** IDH is frequent amongst patients on maintenance hemodialysis in our setting, with various patients related factors associated.

Keywords

Hemodialysis, Intradialytic Hypertension, Incidence, Associated Factors, Cameroon

1. Introduction

Hemodialysis (HD) is a life-sustaining treatment for patients with end stage kidney disease (ESKD) and hypertension (HTN) is a common problem amongst these patients [1] [2]. During HD, blood pressure (BP) changes occur frequently and large variability in BP is a risk factor for increased mortality in these patients [3]. Normally during the dialysis session, BP reduction occurs in most patients, but some patients will in the contrary have a significant increase in BP. This phenomenon called intradialytic hypertension (IDH) is a well-recognized problem amongst patients on HD. No standard definition of IDH exists, but the one with clinical relevance used by many authors is an increase in systolic blood pressure (SBP) of 10 mmHg or more from pre to post-HD blood pressure values [4].

Reported prevalence of IDH ranged from 13.2% to 33.9% (**Figure 1**) and the phenomenon was associated with adverse outcome [5]-[10]. Mortality amongst patients with ESKD is known to be high mainly from cardiovascular origin [2] [11] and studies have shown that IDH is a risk factor for cardiovascular events and death [2] [7] [12]. In the study of Inrig *et al.*, two-year mortality was increased amongst incident patients with IDH and the odd of death and hospitalization at 6 months was increased by 20% in prevalent patients [7] [12]. The cause of IDH is not well established, but volume overload is suggested to be a key factor for its development [13] [14]. Others factors playing a role in his pathogenesis are sympathetic nervous system over-activity [15] [16], activation of the

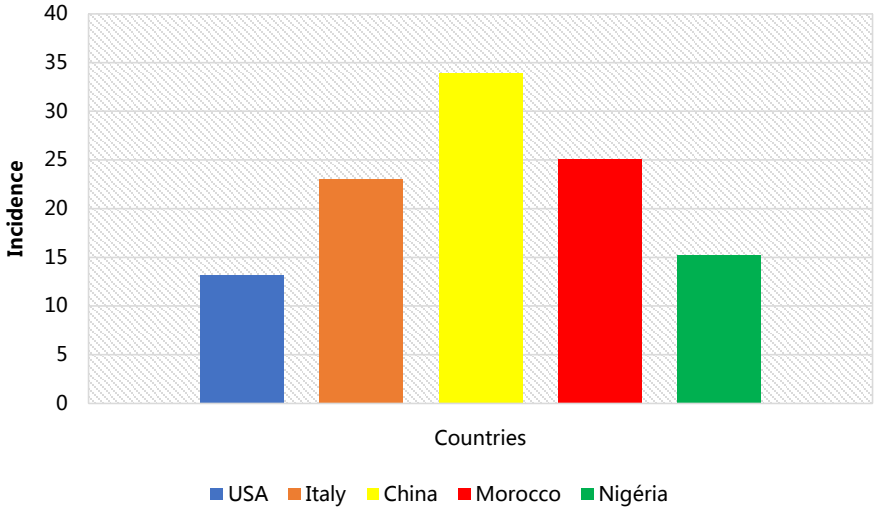

Figure 1. Incidence of IDH by country.

renin-angiotensin-aldosterone system (RAAS), endothelial cell dysfunction [17] [18], changes in sodium, potassium and calcium levels during dialysis [19] [20] [21], removal of antihypertensive medications by the dialysis procedure such as angiotensin converting enzyme (ACE) inhibitors and some beta-blockers [22], and use of erythropoietin stimulating agents (ESA) [23] [24]. Also older age, low dry weight, history of HTN, use of a great number of antihypertensive medications, low serum creatinine and low serum albumin were reported to be associated to IDH [12] [25].

In sub-Saharan Africa in general and in Cameroon in particular, hypertension, a major cause of CKD is highly prevalent in patients with ESKD on HD [26] [27] [28] [29]. HD has been expanded in Cameroon in the last decade with almost 1200 patients on treatment at the end of the year 2016. A study by Kaze *et al.* reported that hypertensive crises defined as any symptomatic increase in SBP of at least 30 mmHg from the value at the beginning of the dialysis session was the 3th leading acute complication amongst patients on HD [27]. Despite the proven adverse outcomes of IDH, data on that phenomenon are inexistent in Cameroon. Therefore, the aim of the present study was to determine the burden of IDH and associated factors amongst patients on maintenance HD in Cameroon.

2. Methods

2.1. Study Setting

We conducted a prospective cohort study in the HD unit of the Douala general hospital (DGH) in Cameroon, from January 2016 to March 2016. DGH is tertiary public institution which serves as referral hospital for patients with kidney diseases for the littoral region of the country [30]. At the time of the study the center was equipped with 20 Fresenius® 4008 S generators (Fresenius Medical Care, Hamburg, Germany), and used synthetic polysulfone dialysis membrane, bicarbonate and a dialysate with 140 Meq/l of sodium. The center operates from Monday to Saturday with 4 shift dialysis per day from 5:00am to midnight. A total of 187 chronic patients were registered, they received 2 dialysis sessions of 4 hours duration each per week. The unit was operating with 2 nephrologists, 1 general practitioner and 12 state registered nurses. Nurses were working in groups according to time schedules: the daytime team (from 6:00 am to 5:00 pm) and the nighttime team (from 5:00 pm to 12:00 pm). Dry weight is assessed by the nephrologists. This study received administrative authorization from the DGH and was approved by the ethic comity of the Douala University, Cameroon. All consenting patients who were following their HD treatment at the DGH where included, while we excluded patients with ESKD who performed temporarily HD session at DGH and those on whom blood pressure measurement was not possible in the arm.

2.2. Data Collection

During the study period, socio demographic, clinical and biological data were

recorded from all consenting ESKD patients and medical records. This included: age, gender, monthly income, comorbidity (HTN, diabetes, left ventricular hypertrophy (LVH), gout, polycystic kidney disease (PKD), Human immunodeficiency virus (HIV), baseline nephropathy, duration on dialysis, number of sessions per week, current medication such as antihypertensive drugs, erythropoietin stimulating agent (ESA) and calcium containing drugs. We monitored dialysis sessions of patients, the follow-up was performed from the 18th of January 2016 to the 31st of March 2016. Data collected on dialysis days were: BP and heart rate during the session, interdialytic interval, presence of edema, dry weight, and weight before and after the session, UF rate, consumption of antihypertensive drugs, blood transfusion and the volume of blood transfused during the session.

At each session BP was measured on the arm without vascular access using an automatic manometer supplied with the dialysis generators (Fresenius® 4008 S). The first measurement was performed five minutes before the beginning of the session, after a resting period of at least fifteen minutes and before the needle insertion. The measurements were then made every hour and the last one at the end of the session before restitution. Heart rate was recorded the same way. Weight measurement was done before and after the dialysis session, the patient dressed the same way with a "SOENLHE 7708" electronic scale.

For each participant 3 ml of blood was collected at the beginning of the study for albumin dosage in the biochemistry laboratory of the DGH using an automat Cobas 311. An electrocardiogram was performed after the first dialysis session with a CARDIART 6108T to search for left ventricular hypertrophy (LVH) using Sokolow index (S wave depth in V1 + tallest R wave height in V5 or V6 > 35 mm) [31].

2.3. Definitions

IDH was defined as an increase of at least 10 mmHg in SBP between the beginning and the end of the dialysis session.

Interdialytic interval was the number of days between two successive dialysis sessions.

Interdialytic weight gain was the difference between patient's weight at the beginning of the session and the weight at the end of the previous session. Incidence of IDH was expressed by multiplying the number of sessions with IDH by 100 over the total number of sessions followed.

Etiology of CKD was mainly done clinically in the absence of renal histology.

A treatment was considered regular when a patient follows it as prescribed by the treating physicians.

2.4. Statistical Analysis

Data were analyzed using STATA 12.0. Quantitative variables were expressed as average with the standard deviation or median and compared with the Wilcoxon test. Categorical variables were expressed in numbers and percentages and then

compared using the Fischer test. The search for associated factors was done using univariate logistic regression model. Data with a p-value equal or less than 20% were then included in a bivariate analysis by adjusting the different input data. A p value < 0.05% was considered statistically significant.

3. Results

3.1. General Characteristic of the Study Participants

A total of 176 patients were followed during 1981 dialysis sessions, with an average of 11.26 ± 2.49 sessions per patient. The mean age of participants was 49.06 ± 13.9 years, 64.2% (113/176) were male and 50.5% of patients (89/176) had a monthly income < 35,000 XAF. The prevalence of HTN was 89.7% (158/176) with 137/158 on antihypertensive drugs amongst which only 46.7% (64/137) followed regular treatment. Diabetes was more common in males (p = 0.001) while female were more HIV positive (p = 0.014). The median duration on HD was 26.5 months (range: 1 - 396). Clinical characteristics are summarized in Table 1.

Table 1. Sociodemographic and clinical characteristics of the study population.

Variable	Overall	Men	Women	p-value
Number	176	113	63	-
Mean age ± SD	49.06 ± 13.97	50.69 ± 13.89	46.15 ± 13.73	0.054
Monthly income < 35000 n (%)	89 (50.57)	38 (33.63)	51 (80.95)	<0.001
Arterio-venous fistula n (%)	165 (93.75)	103 (91.15)	62 (98.41)	0.100
Mean duration on dialysis (months)	26.5	26	27	1.000
Two weekly sessions n %	171 (97.16)	110 (97.35)	61 (96.83)	1.000
Comorbidities				
Hypertensionn (%)	158 (89.77)	103 (91.15)	55 (87.30)	0.444
HTN mean duration ± SD (years)	9.09 ± 6.62	8.91 ± 6.64	9.44 ± 6.62	0.624
HTN treatment n (%)	137(86.71%)	-	-	-
HTN with regular treatment n (%)	64 (46.72%)	-	-	-
Diabetes n (%)	34 (19.32)	30 (26.55)	4 (6.35)	0.001
Left ventricular hypertrophy n (%)	96 (54.55)	57 (50.44)	39 (61.90)	0.158
HIV n (%)	13 (7.39)	4 (3.54)	9 (14.29)	0.014
Gout n (%)	10 (5.68)	9 (7.96)	1 (1.59)	0.098
Use of ESA n (%)	42 (23.86)	29 (25.66)	13 (20.63)	0.580
Use of calcium n (%)	131 (74.43)	86 (76.11)	45 (71.43)	0.589
Background nephropathy n (%)				
Nephroangiosclerosis	29 (16.48)	23 (20.35)	6 (9.52)	0.089
Diabetes Nephropathy	25 (14.20)	21 (18.58)	4 (6.35)	0.026
HIV	10 (5.68)	4 (3.54)	6 (9.52)	0.170
Chronic glomerulonephritis	43 (24.43)	28 (24.78)	15 (23.81)	1.000
Chronic interstitial nephritis	9 (5.11)	5 (4.42)	4 (6.35)	0.723
Polycystic kidney disease	2 (1.14)	0 (0.00)	2 (3.17)	0.127
Unknown	58 (32.95)	32 (28.32)	26 (41.27)	0.095

SD: standard deviation, HTN: hypertension, HIV: human immunodeficiency virus.

3.2. Incidence of IDH and Associated Factors

The incidence of IDH was 48.3% (Figure 2) and was higher in women compared to men (p = 0.01). A total of 71.18% (1410/1981) HD sessions followed were initiated with BP ≥ 140/90 mmHg. The characteristics of the sessions are summarized in Table 2. During the study, 93.7% (165/176) patients had at least one episode of IDH with a median of 5 episodes per patient (range 0 - 12). In bivariate analysis, factors that increase the risk of IDH were HTN (p = 0.004; RR = 1.3), male gender (p = 0.038; RR = 1.14), monthly income < 35,000 XAF (p = 0.028; RR = 1.13), blood transfusion during the session (p < 0.001; RR = 1.57) and use of ≥2 antihypertensive drugs (p < 0.001; RR = 1.27). Factors associated with lower risk were age ≥ 50 years (p = 0.012; RR = 0.86), longer duration on dialysis ≥ 30 months (p < 0.001; RR = 0.8), dry weight ≥ 67 kg (p < 0.001; RR = 0.77), UF rate ≥ 800 ml/h (p < 0.001; RR = 0.71) and BP at the beginning of the session ≥ 140/90 mmHg (p < 0.001; RR = 0.56) (Table 3).

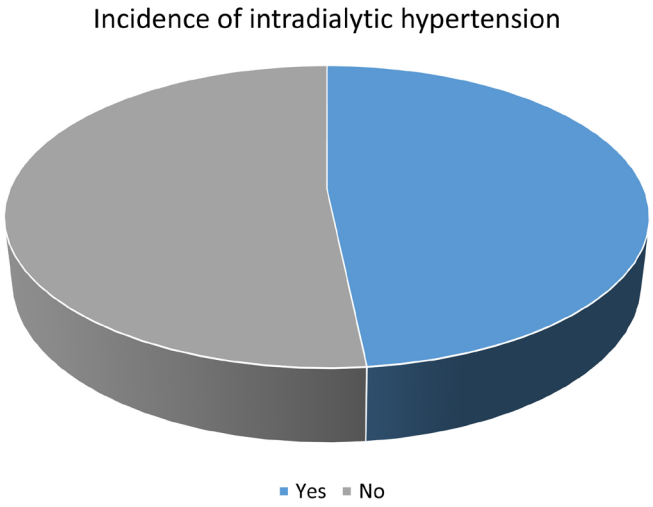

Figure 2. Incidence of IDH.

Table 2. General characteristics of dialysis sessions.

Variable	Overall	Men	Women	p-value
Number	1981	1261	720	-
Mean ± SD	11.26 ± 2.49	11.16 ± 2.68	11.43 ± 2.13	0.655
Mean SBP at the beginning ± SD	154.25 ± 23.60	155.10 ± 24.05	152.74 ± 22.87	0.37
Mean SBP at the end ± SD	162.68 ± 24.91	162.08 ± 22.03	163.75 ± 29.54	0.70
Mean DBP at the beginning ± SD	81.69 ± 15.29	81.17 ± 16.61	82.61 ± 12.64	0.55
Mean DBP at the end ± SD	86.60 ± 15.12	86.19 ± 15.58	87.32 ± 14.35	0.65
BP at beginning ≥ 140/90 mmHg n (%)	1410 (71.18)	949 (75.26)	461 (64.03)	<0.001
ΔSBP > 10 mmHg at any moment n (%)	1297 (65.47)	802 (63.60)	495 (68.75)	0.021
Edema n (%)	252 (12.72)	177 (14.04)	75 (10.42)	0.021
Blood transfusion n (%)	88 (4.44)	44 (3.49)	44 (6.11)	0.009

DS: standard deviation; SBP: systolic blood pressure; DBP: diastolic blood pressure; ΔSBP: postdialysis SBP minus predialysis SBP.

Table 3. Associated factors to intradialytic hypertension.

Variable	RR	CI 95%	p-value
Male gender	1.14	1.01 - 1.26	0.038
Age ≥ 50 years	0.86	0.76 - 0.97	0.012
Monthly income < 35,000 XAF	1.13	1.01 - 1.25	0.028
Hypertension	1.30	1.10 - 1.48	0.004
Left ventricular hypertrophy	1.05	0.94 - 1.17	0.358
Use of ESA	1.01	0.88 - 1.13	0.926
Duration on dialysis ≥ 30 months	0.80	0.71 - 0.90	<0.001
Gout	0.79	0.59 - 1.01	0.058
Dry weight ≥ 67 kg	0.77	0.67 - 0.88	<0.001
Ultrafiltration rate ≥ 800 mL/h	0.71	0.60 - 0.81	<0.001
Heart rate ≥ 75 bpm	1.08	0.98 - 1.18	0.105
BP at the beginning ≥ 140/90 mmHg	0.56	0.46 - 0.66	<0.001
Blood transfusion	1.57	1.33 - 1.75	<0.001
Number of antihypertensive drugs ≥ 2	1.27	1.15 - 1.38	<0.001

BP: blood pressure. ESA: erythropoietin stimulating agents.

4. Discussion

The aim of this study was to determine the incidence and factors associated to IDH amongst ESKD patients in Cameroon. We found that our patients were relatively young adults, mainly men and hypertension was the main comorbidity affecting 9 of 10 patients. IDH was frequent with an incidence of 48.3%. Factors associated with increased risk of IDH were HTN, male gender, low monthly income, blood transfusion during the session and use of 2 or more antihypertensive drugs. Factors associated with lower risk were age ≥ 50 years, longer duration on dialysis, dry weight ≥ 67 kg, high UF rate and high BP at the start of dialysis session.

Elevation of BP during HD is a frequent but an ignored phenomenon amongst patients on HD. Clinicians focus more on intradialytic hypotension and its complications because it is more symptomatic, despite the proven adverse outcome of IDH namely the increased risk of hospitalization and death [12]. This study revealed that IDH is very frequent amongst patients on HD in Cameroon with an incidence of 48.3%. The reported prevalence of IDH varies depending on the number of HD treatments in which BP measurements occur and the definitions used. Our result is one of the highest compared to the reported incidence in the literature [5]-[10]. Considering IDH as an increase at least 10 mmHg from pre to post-HD mean SBP from all sessions, Inrig *et al.* reported a prevalence of 13.2% in a retrospective study where prevalent HD patients were assessed over 4 HD sessions, and a prevalence of 12.2% was found in incident one when BP measurements were assessed over 2 weeks [7] [12]. Amira *et al.* in Nigeria re-

ported a prevalence of 15.2%, defining IDH as an increase of BP during the second or third hour after significant ultrafiltration [5], but in that study the level of BP to define IDH was not clear also the definition of significant UF.

Using the same definition as in the present study, Van Buren *et al.* found a prevalence of IDH of 21.3% after a 6 months assessment of BP measurements during HD treatments. In that observational study, almost every patient experienced at least one episode of IDH, but it occurred in 31.3% of treatments [9]. The high prevalence found in our study can be mainly explained by the fact that our patients received only 2 dialysis sessions of 4 hours weekly instead of 3 per week as in the majorities of studies. Consequently control of extracellular volume and dry weight is difficult to achieve. Studies have shown that dry weight reduction lowers intradialytic BP [13] [32] [33]. Also in the present study, IDH was considered for a single session while in most reported studies mean SBP over the entire period of follow-up was used to define the prevalence of IDH [4] [7] [8] [9] [10], leading to an underestimation of the frequency IDH, which is intermittent in some patients as demonstrated by Van Buren *et al.* [9]. Another possible explanation to the high incidence of IDH is that our participants were all from African ancestry, and it is well known that endothelial dysfunction is more frequent in this population and also play a key role in pathogenesis of IDH [34] [35] [36]. Given the known reported adverse outcome of IDH, the finding of this study raised the need of actions to reduce the burden in our setting.

Factors independently associated with increased risk of IDH in this study were male gender, low income, HTN, blood transfusion during the session and use ≥ 2 antihypertensive drugs. While the risk was low in older patients, longer duration on dialysis, high dry weight, high UF rate and high BP at the start of the dialysis session. Reported factors that increased the risk of IDH are older age, HTN, low dry weight, higher intradialytic weight gain, lower UF rate, lower SBP at the beginning of the session, short time on HD treatment, high number of antihypertensive medications, low serum creatinine and low albumin [4] [7] [8] [10] [12]. The role of HTN can be due to the modification of the endothelium which occurred with time and also maybe a sign of sympathetic over-activation or greater stimulation of the RAAS [25]. Blood transfusion while bringing new volume is responsible of expansion and then increases BP, while a greater UF rate reduces fluid and then decrease BP. A lower dry weight can be a consequence of a better fluid status preventing fluid overload [13] [25] [35].

We found that older age reduced the risk of IDH while male gender increased the risk. These findings are not reported in the literature and may suggest specific characteristics of our population that need further investigations. The role of specific agents should be determined and all these factors need to be considered in order to reduce the rate of IDH in our setting [23] [24]. One major measure is to reduce dry weight as this is reported to improve IDH over time in some patients [13] [32] [35]. Avoiding dialyzable antihypertensive medications and prefer non dialyzable RAS inhibitors, and administration of ESA subcuta-

neous can also be considered. Patients should be educated to minimize salt and fluid intake between HD sessions. Also increasing the number of dialysis sessions of our patients could be a major step, hence studies have shown that frequent HD reduces BP and the number of prescribed antihypertensive medications [29] [33] [35] [37].

5. Conclusion

We found that IDH is very frequent in our setting affecting almost half of the study population. It is more common in male, young patients, those with HTN, low income, who received blood transfusion during sessions, had a short duration on HD, a lower UF and high BP at the beginning of session. Patients were also found to have higher dry weight and many antihypertensive medications. This raises the need of specific measure for the care of affected patients. Further studies are necessary to determine the consequences of IDH in our setting and orientate the treatment of affected patients.

Limitations

No consensual definition of IDH exists; in the present study we used an increase of 10 mmHg between pre and post dialysis BP for each session. This can lead to overestimation of the phenomenon considering that it is intermittent in some patients, and therefore, it can be less effective to determine the real factors associated with the persistent IDH. It was a single center study, the result can't be generalized. The major strength is that this study describes for the first time the burden of IDH in an SSA setting where HTN is a major cause of CKD and results can help to take action to reduce the burden amongst our patients.

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Conflicts of Interest

No relevant conflict of interest.

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