Impact of Metabolic Acidosis on the Dialysis Dose: Findings from a two center cross-sectional study in a low income population setting

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Summary

BACKGROUND

Metabolic acidosis (MA) still remains a very common finding in patients with end stage kidney disease (ESRD) despite the increasing volume of research on dialysis treatment that have resulted in improved haemodialysis delivery. Its occurrence increases the risk of dialysis termination and inadequate dialysis dose that is associated with poor treatment outcome. The study endeavored to study metabolic acidosis and to determine its relationship with the dialysis dose (Kt/V).

MATERIALS AND METHODS

This was a two centre cross-sectional study involving 298 participants with ESKD who had 1642 sessions of maintenance haemodialysis. Serum electrolytes were analyzed by the Ion-Selective Electrode method and haematocrit was determined using a Hematocrit Centrifuge.

RESULTS

Two hundred and ninety eight (192 males and 106 females) participants took part with a mean age of 51.44 ± 7.31 years (males, 51.18 ± 4.62 years, females, 52.14 ± 2.93 years), P=0.04. The mean serum bicarbonate concentration, post dialysis (20.61 ± 6.26 mmol/L) was significantly higher than the pre dialysis, 18.41 ± 3.63 mmol/L (P<0.001) concentration. The prevalence of pre and post dialysis metabolic acidosis were 79.0% and 38.3% (P<0.001). There was a significant reduction in the mean anion gap following dialysis (P<0.001). The mean dialysis dose was significantly higher in males than females (P=0.03) and in participants with normal PSBC than participants with low PSBC (P<0.001). Risk factors for metabolic acidosis were advancing age, elevated Body Mass Index and blood pressure. Metabolic acidosis was negatively related to glomerular filtration rate and haematocrit. Aging, lesser dialysis frequency, independently predicted metabolic acidosis.

CONCLUSION

Metabolic acidosis is quite common in patients on maintenance dialysis, more common in females, advancing age and in less frequent dialysis treatment. Its occurrence increased the risk of inadequate dialysis.

Keywords: *Metabolic Acidosis, Anion Gap, Maintenance Haemodialysis, Dialysis Dose, Predialysis serum Bicarbonate Concentration.*

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Introduction

Metabolic acidosis (MA) still remains a major finding in many patients on maintenance haemodialysis (MHD) despite significant knowledge and improvements in dialysis delivery [1]. It results from declining kidney function leading to reduction in non-volatile acid excretion (NAE) coupled with low tubular bicarbonate generation. Factors implicated in the high prevalence of MA in the dialysis population include inadequate dialysis, increased intake of animal protein, drugs particularly non-loop and non-thiazides diuretics, and phosphate binders. A positive correlation is reported between MA and anion gap (AG) [2].

Metabolic acidosis, defined as low serum bicarbonate concentration (SBC), in chronic kidney disease (CKD), presents commonly at a glomerular filtration rate (GFR) of $\leq$40 ml/min after hyperparathyroidism and anemia, and is followed by hyperkalemia and hyperphosphatemia [3]. Apart from its suppressive effect on cardiac contractility, MA induces systemic and cutaneous vasodilatation leading to intradialysis hypotension (IDH) which reduces the effective blood volume (EBV), the dialysis blood flow rate (BFR) and ultimately inadequate dialysis [4].

Raikou *et al* found MA as a risk factor for intradialysis hypertension and poor dialysis outcome [5] as it also increases the risk of protein energy malnutrition (PEM), abnormal hormonal profile, and CKD mineral bone disease (CKD-BMD) [1,2]. MA is associated with inadequate dialysis which can impact negatively on quality of life (QOL), morbidity and mortality [2,5].

Serum bicarbonate concentration (SBC) is determined by estimating total serum carbon dioxide or by arterial blood gases, using the Henderson-Hasselbalch equation. Results of SBC assessment could be affected by time between collection and analysis, and by sample transporting medium [6].

MHD is routinely given thrice weekly in developed nations but twice weekly or less in most low income nations (LINs) [5,7]. MA in MHD is well studied in developed nations, including its relationship with dialysis dose [4] however, literature is rather scarce in low income nations. We, therefore, studied metabolic acidosis, and determined its relationship with the dialysis dose (Kt/V).

Materials and Methods

Study design

This two centre cross sectional study was conducted at the Federal Medical Centre (January-December 2017), Abeokuta and Babcock University Teaching Hospital, Ilishan-Remo (November 2018-August 2020), both in Ogun State, Nigeria.

Study population

There were 298 (192 males and 106 females) consented participants, 16 years or

older who had ESKD, according to the KDOQI 2012 criteria [8], and receiving MHD. They were consecutively recruited. Participants' data were collected after been on MHD for at least a month. A total 310 participants took part from the two centres but data for 12 were missing, so data of 198 were analyzed. Between 4 and 6 dialysis sessions were studied in each participant. Participants with kidney transplant, pelvic tumors, infections or with HD sessions less than once weekly were excluded.

Data collection

Data was collected from history and participant case notes and dialysis charts and entered into a case report form. Variables retrieved were age, gender, history of pharyngitis or skin sepsis in childhood and adolescence and aetiology of CKD.

Predialysis review

Height and weight were measured with participants on very light clothing without shoes, cap or head gear and the Body Mass Index (BMI) calculated. At each session, the difference between the predialysis weight and the post dialysis weight of the preceding session was taken as the interdialytic weight gain (IDWG). The predialysis vital signs (percentage oxygen saturation (SPO_2) pulse rate (PR) and BP), were taken after 5 minutes of rest, and were repeated half hourly up to 30 minutes post dialysis. All BP readings were taken manually. The IDWG, vital signs and the aetiology of CKD were used as a guide to prescribe the dialysis dose. Temperature was normal at the commencement of all dialysis sessions.

For participants with the internal jugular catheter, 0.5-1 milliliter of blood was withdrawn through the catheter and discarded to confirm its patency, predialysis samples were taken and both arterial and venous ends were flushed with heparinized saline. For arteriovenous fistula (AVF), blood samples were withdrawn from a vein in the contralateral arm, and for femoral catheters, blood was taken from newly sited catheters (according to unit protocol). When the risk of bleeding was high, heparin dose was reduced depending on the clotting profile result.

Dialysis procedure

Participants were connected first through the arterial and then the venous portal. Where the blood flow rate (BFR) was reduced to manage IDH or increased to improve the targeted dialysis dose, the mean was calculated. When there was an intradialysis rise in temperature up to 1^0C and the PR up to 120/minute with a concurrent decrease in BP, blood flow rate (BFR) was reduced by 50 ml/min (down to a minimum of 250ml/min) to reduce the risk of IDH and possible arrhythmias.

When IDH or IDHT occurred, vital signs were taken quarter hourly. For all dialysis sessions, the dialysate flow rate (DFR) was 500ml/min and bicarbonate buffer was used, with a dialysate fluid concentration of 34 mmol/L.

Post dialysis management

The stop dialysate flow method for the collection of the post dialysis blood sample was used. At the end of dialysis time, dialysate flow was stopped and blood pump was reduced to 100 ml/min. Five minutes after stopping the dialysate flow, blood was taken from the arterial portal, for serum electrolytes (to minimize access recirculation) and then, the haematocrit.[9] Urea reduction ratio (URR) was calculated using the pre and post dialysis urea while Kt/V were calculated from the Daugirdas second generation logarithmic estimation of single pool, using the pre and post dialysis urea, ultrafiltration volume, post dialysis weight and dialysis duration [10].

The URR and Kt/V were related by the equation, Kt/V = In (1-URR), where In is natural log [11].

Sample processing

Analysis of serum sodium, potassium, chloride, bicarbonate, urea and creatinine was done using the Ion Selective Electrode method while 3ml of blood was taken into another Lithium heparin bottle for determination of serum albumin (index dialysis for each participant) using the bromocresol green method. The bromocresol green method overestimates albumin by about 3.5g/dL in renal diseases including dialysis patients. Therefore, cut-off values for normal serum albumin were raised by about 3-3.5 or 5.5-7 g/dl compared to the bromocresol purple or the immunophelometric assay, respectively [12]. The haematocrit [(HCT) was determined using a Haematocrit Centrifuge.

Although SBC <22 mmol/L is mostly used as marker of MA, in our study, we used the value of <20 mmol/L according to local laboratory reference values. All participants stopped taking major meals 2 hours prior to commencement of dialysis as part of the unit protocol to reduce the risk of IDH. The mean of all variables over a monthly assessment was used for each participant throughout the study [13].

Ethical considerations

This study was approved by the Human Ethics Committees of the Federal Medical Centre, Abeokuta (FMCA/470/HREC/03/2017) and Babcock University, Ilishan-Remo (BUHREC/723/19), and followed the tenets of the Helsinki 1973 declaration [14] as revised in 2000.

Statistical analyses

Data generated from the study was analyzed using Statistical Package for Social Sciences (SPSS) software version 22.0 (IBM, CA, USA). Continuous variables were presented as means with standard deviation and compared using t-test while categorical variables were presented as proportions and compared using Chi square test or fisher's exact test. The P-value <0.05 was considered statistically significant.

ANOVA was used to compare the means of 3 or more continuous variables. A univariate regression analysis assessed the strength of association between reduced PSBC (<20mmol/l) and participant variables (Table 5), and variables with P<0.025 were entered into a multiple regression model to determine independent predictors of reduced PSBC using backward elimination to adjust for confounders (Table 6). Hosmer *et al* [18] found that the use of P<0.05 did not commonly identify all important variables.

Results

Two hundred and ninety eight participants (192 male and 106 females who had 1642 dialysis sessions (Table 1) were studied. The mean age of all participants was 51.44 $\pm$ 7.31 yrs (males 51.18 $\pm$ 4.62 yrs, females, 52.14 $\pm$ 2.93 yrs), P=0.04. A greater proportion (40.6%) of participants had HACKD.

The mean predialysis BMI, SPO_2, SBP, and DBP were 24.73 kg/m^2, 94.66%, 162.45 mmHg and 99.82 mmHg respectively. At commencement, hypoxaemia, systolic and diastolic hypertension was found in 88.1%, 84.2% and 87.0% of the sessions respectively.

The mean predialysis BMI, systolic and diastolic BP were significantly higher than the post dialysis values, P=0.04, P<0.001 and P=0.002 but the mean predialysis SPO_2 was significantly lower than the post dialysis, P=0.02.

Table 1: Socio-Demographic and Historical Characteristics of Participants

Variables	Frequency N=298 (%)	Dialysis sessions N=1642 (%)
Gender		
Males	192 (64.4)	1064 (64.8)
Females	106 (35.6)	578 (35.2)
Age, *years*		
16-44	109 (36.6)	527 (32.1)
45-74	173 (58.0)	1064 (64.8)
≥75	16 (5.4)	51 (3.1)
Etiology of CKD		
Hypertension	121 (40.6)	734 (44.7)
Chronic glomerulonephritis	109 (36.6)	673 (41.0)
Diabetes	36 (12.1)	127 (7.7)
Obstructive uropathy	16 (5.4)	69 (4.2)
Polycystic kidney disease	10 (3.3)	22 (1.4)
Others	6 (2.0)	17 (1.0)
Dialysis sessions/week		
1	103 (34.6)	550 (33.5)
≥2	195 (65.4)	1092 (66.5)
Erythropoietin 4000 IU/week		
1	89 (29.9)	524 (31.9)
≥2	209 (70.1)	1118 (68.1)

*CKD-chronic kidney disease, IU-international unit

Table 2: Comparison between the Pre and Post Dialysis Laboratory Characteristics of Participants

Variables	Pre dialysis Mean ± SD	Post dialysis Mean ± SD	t-test	P-value
Sodium, *mmol/l*	129.3 ± 4.2	133.8 ± 2.3	0.8	0.06
Potassium, *mmol/l*	5.5 ± 1.3	4.1 ± 1.1	5.8	<0.001
SBC, *mmol/l*	18.4 ± 3.6	20.6 ± 6.3	5.6	<0.001
SBC (males), *mmol/l*	19.0 ± 6.8	21.1 ± 4.3	4.1	<0.001
SBC (females), *mmol/l*	17.3 ± 6.2	19.7 ± 2.7	5.8	<0.001
Chloride, *mmol/l*	99.1 ± 2.7	100.6 ± 7.4	1.0	0.05
Calcium, mmol/l	2.1 ± 1.2	2.3 ± 1.4	5.0	0.001
Phosphate, *mmol/l*	2.1 ± 1.8	1.8 ± 0.4	5.4	<0.001
Urea, *mmol/l*	19.7 ± 3.9	8.9 ± 3.1	10.8	<0.001
Creatinine, *umol/l*	842.7 ± 18.4	417.7 ± 18.3	9.7	<0.001
GFR, *ml/min*	6.9 ± 2.1	11.8 ± 3.5	8.8	<0.001
Haematocrit, *%*	24.3 ± 4.3	25.7 ± 7.3	0.9	0.08
Anion gap, *mEq/L*	27.5 ± 6.7	16.9 ± 7.2	7.2	<0.001
Anion gap (males), *mEq/L*	26.9 ± 2.5	16.2 ± 5.5	6.9	<0.001
Anion gap (females), *mEq/L*	28.7 ± 7.3	18.2 ± 3.6	6.1	<0.001

*SBC-serum bicarbonate concentration, GFR- glomerular filtration rate

Table 3: Relationship between Predialysis Bicarbonate and Content of the Prescribed Dialysis

Variables	All sessions N=1642 (%)	PSBC, *mmol/l* <18.0 N=493 (%)	PSBC, *mmol/l* 18.0-19.9 N=804 (%)	PSBC, *mmol/l* ≥20.0 N=345 (%)	P-value
Blood flow rate, *ml/min*					
<350.0	435 (26.49)	182 (36.92)	206 (25.62)	47 (13.62)	<0.001
≥350.0	1207 (73.51)	311 (63.08)	598 (74.38)	298 (86.38)	
Dialysis duration, *hours*					
<4	87 (5.30)	59 (11.97)	21 (2.61)	7 (2.03)	0.001
4	1555 (94.70)	434 (88.03)	783 (97.39)	338 (97.97)	
Dialyzer surface area, m^2					
1.7	1492 (90.86)	467 (94.73)	727 (90.42)	298 (86.38)	0.003
1.8	150 (9.14)	26 (5.27)	77 (9.58)	47 (13.62)	
Ultrafiltration volume, *L*					
<3.0	922 (56.15)	112 (22.72)	513 (63.81)	297 (86.09)	0.04
≥3.00	720 (43.85)	381 (77.28)	291 (36.19)	48 (13.91)	
Dialysis catheter					
AVF	346 (21.07)	49 (9.94)	203 (25.25)	94 (27.25)	0.001
Tunneled IJV	728 (44.34)	174 (35.30)	386 (48.01)	168 (48.70)	
Non-tunneled IJV	135 (8.22)	47 (9.53)	63 (7.84)	25 (7.24)	
Femoral	433 (26.37)	223 (45.23)	152 (18.90)	58 (16.81)	

*PSBC-predialysis serum bicarbonate concentration, AVF-artero-venous fistula, IJV-internal jugular vein

Table 4: Relationship between Predialysis Serum Bicarbonate and Dialysis Outcome

Variables	All sessions N=1642 (%) Mean ± SD	SBC, *mmol/l* <18.00 N=493 (%) Mean ± SD	SBC, *mmol/l* <18.00-19.99 N=804 (%) Mean ± SD	SBC, *mmol/l* ≥20.00 N=345 (%) Mean ± SD	P-value
Intradialysis death	2 (0.12)	0 (0.0)	1 (0.12)	1 (0.29)	<0.001*
Terminated dialysis	87 (5.30)	42 (8.52)	37 (4.60)	8 (2.32)	<0.001
Kt/V					
Mean	1.14 ± 0.51	0.98 ± 0.32	1.13 ± 0.64	1.41 ± 1.75	<0.001
<1.2	1427 (86.91)	484 (98.17)	706 (87.81)	237 (68.70)	<0.001
≥1.2	215 (13.09)	9 (1.83)	98 (12.19)	108 (31.30)	
URR, *%*					
Mean	59.64 ± 12.03	54.25 ± 8.92	59.11 ± 8.84	68.59 ± 11.88	<0.001
<65	1398 (85.14)	477 (96.75)	710 (88.31)	234 (67.63)	<0.001
≥65	244 (14.86)	16 (3.25)	94 (11.69)	111 (32.37)	

*SBC-serum bicarbonate concentration, *-fisher's exact test, Kt/V-urea clearance as a function of distribution volume, URR- urea reduction ratio

The mean predialysis sodium, chloride, calcium and GFR were lower than the mean post dialysis concentrations, (P=0.06), chloride (P=0.05), calcium (P=0.001) and (P<0.001) respectively. The mean predialysis potassium, phosphate, urea, creatinine and anion gap were higher than the post dialysis concentrations, (P<0.001), (P<0.001), (P<0.001), (P<0.001) and P<0.001 respectively (Table 2).

The mean PSBC was significantly less than the post dialysis SBC, (P<0.001) but was significantly higher in males than in females, P=0.04. Ninety seven percent of the dialysis sessions were commenced with PSBC <20.00 mmol/L, which became 38.3% post dialysis.

The mean serum albumin at the commencement of study, for all participants, males and females were 33.60 ± 4.32 g/dl, 34.92 ± 3.54 g/dl and 30.91 ± 3.1g/dl (P=0.003).

Table 5: Univariate Analysis of Factors Associated with Reduced PSBC

Variables	**SBC, *mmol/l* <20.00 N=1297 (%) Mean ± SD**	**SBC, *mmol/l* ≥20.00 N=345 (%) Mean ± SD**	**P-value**
Gender			
Males (n, %)	833 (78.29)	231 (21.71)	0.04
Females (n, %)	464 (80.28)	114 (19.72)	
Age, *years*			
16-44	370 (70.21)	157 (29.79)	<0.001
45-74	885 (83.18)	179 (16.82)	
≥75	42 (82.35)	9 (17.65)	
Etiology of CKD			
Hypertension (n, %)	584 (81.80)	130 (18.20)	0.6
Chronic glomerulonephritis (n, %)	530 (78.40)	146 (21.60)	
Diabetes (n, %)	97 (72.93)	36 (27.07)	
Others (n, %)	86 (72.27)	33 (27.73)	
Dialysis sessions/week			
1 (n, %)	526 (95.63)	24 (4.37)	<0.001
≥2 (n, %)	771 (70.60)	321 (29.40)	
Erythropoietin 4000 IU/week			
1	463 (88.4)	61 (11.6)	0.002
≥2	834 (74.6)	284 (25.4)	
Mean BMI, kg/m^2	24.97 ± 12.41	23.82 ± 9.53	0.1
Mean SPO_2, *%*	93.95 ± 10.43	97.33 ± 15.48	<0.001
Mean SBP, *mmHg*	167.52 ± 9.55	143.39 ± 8.25	<0.001
Mean predialysis creatinine, *umol/L*	892.17 ± 22.47	656.53 ± 18.36	<0.001
Mean predialysis GFR, *ml/min*	6.73 ± 3.42	7.78 ± 4.65	0.001
Haematocrit, *%*	23.01 ± 1.04	29.34 ± 2.14	<0.001
Kt/V	1.07 ± 0.2	1.41 ± 0.75	<0.001
URR,%	57.26 ± 2.25	68.59 ± 11.88	<0.001

*PSBC-predialysis serum bicarbonate concentration, CKD-chronic kidney disease, BMI-body mass index, SPO2-percentage oxygen saturation, SBP-systolic blood pressure, DBP-diastolic blood pressure, GFR-glomerular filtration rate

Of the 1427 sessions with inadequate dialysis, 33.91% had VL-PSBC and 49.47% had L-PSBC. Of the 215 sessions with adequate dialysis dose, 50.23% had normal PSBC and 45.58% had L-PSBC. Univariate analysis showed males had significantly higher mean PSBC than females (P=0.04), (Table 5). The PSBC was negatively correlated with age, systolic BP and serum creatinine (P<0.001), (P=0.002) and (P= 0.002). Participants with CGN had insignificant higher mean PSBC than those with HACKD (P=0.6).

Table 6: Multivariate Regression Analysis

Variables	OR	95% CI	P-value
Age	0.04	0.039-0.051	0.06
Dialysis sessions/week	7.72	4.59-8.32	<0.001
Erythropoietin	4.82	4.86-6.18	0.06
SPO_2	3.18	2.04-9.64	<0.001
Systolic BP	4.33	4.26-6.99	0.03
Creatinine	0.23	0.12-2.53	0.001
Glomerular filtration rate	3.42	2.32-3.52	0.04
Haematocrit	0.02	0.01-1.95	<0.001

*OR-odd ratio, CI-confidence interval, SPO_2-percent oxygen saturation, BP-blood pressure

The determinants of PSBC were dialysis frequency, dialysis dose, predialysis SPO_2, haematocrit and the GFR, (P<0.001), (P<0.001), (P<0.001), (P<0.001) and P=0.001 respectively. Multivariate regression analysis showed infrequent dialysis (OR-7.72, CI-4.59-8.32), SPO_2 (OR-3.18, CI-2.04-9.64), systolic BP (OR-4.33, CI-4.26-6.99), creatinine (OR-0.23, CI-0.12-2.53), GFR (OR-3.42, CI-2.32-3.52) and haematocrit (0.02, CI-0.01-1.95) independently predicted metabolic acidosis in the dialysis population (Table 6).

Discussion

The prevalence of metabolic acidosis (MA) in MHD population at presentation for dialysis in our study was 79.0% (using a serum bicarbonate of 20 mmol/l as threshold). This was reduced to 38.3% post dialysis. The risk factors for MA we found included infrequent dialysis, gender (females), aging, increasing BMI and blood pressure, while MA was a risk factor for IDH, dialysis termination and inadequate dialysis. We also found a positive relationship between predialysis MA and serum creatinine and potassium, and a negative relationship with SPO_2, sodium, haematocrit and GFR. This prevalence is higher than Sajgure [19] *et al* 's prevalence of 62.85%.

Considering the fact that we used a SBC of <20 mmol/L as threshold, it is very probable that our prevalence would have been much higher using a SBC threshold of <22 mmol/L, even higher than the 80% found by Raphael *et al* [20] in the CRIC study, among participants in CKD stage 5, (using a SBC of <22 mmol/L). This fact is further supported by the prevalence of 97% found by Oliveira *et al* [21] in Brazil, a developing country, using a SBC cut-off of 22 mmol/L. We, therefore, inferred that the prevalence of MA in the MHD population in our environment would actually be higher justifying the KDOQI recommendation of a minimum predialysis SBC target of 22 mmol/L [22].

We found a male predominance in the MHD population, a common finding worldwide

but the wider gender margin compared to studies from the advanced nations is in support of findings in local study that found a female bias in accessing health care in LINs due to discriminatory socioeconomic and cultural beliefs and practices [7, 23]. The higher mean age of females in this study agrees with findings by Casimir *et al* [24] who reported that women commence dialysis treatment later than men. Though women are reported to survive better in acute inflammatory conditions, their survival advantage over men is reported to be lost during MHD [25].

There was a direct relationship between MA and the age of participants in our study and agrees with findings by Fressetto *et al* [26] who also reported that MA, particularly if of renal origin accelerates the aging process. During aging, the higher elucidation of inflammatory cytokines mediates tissue destruction and proteolysis leading to the release of metabolites that favours acidosis. Metabolic acidosis was directly related to BMI, similar to findings by Oliviera *et al* [21]. Obesity may be uncommon in MHD due to widespread use of high flux dialyzers, but its occurrence could be associated with the hypoventilatory syndrome, that is made worse in the supine position (common during dialysis) due to the closure of the terminal airways [27].

The positive relationship between MA and the blood pressure in our study is also reported by Adamczak *et al* [2] who, on behalf of the Polish Society of Nephrology, reported that the correction of acidosis in CKD with sodium chloride unlike sodium bicarbonate leads to BP elevation. We found that plasma sodium and potassium were positively and negatively related to the PSBC respectively, supportive of findings by Harris *et al* [28] who reported that hyperkalemia induces MA secondary to reduced tubular ammonia generation and collecting duct ammonia transport. The use of renin angiotensin aldosterone system (RAAS) inhibitors in MHD population, could lead to potassium and acid retention and low sodium, typical of MA in advance kidney disease. There was a positive relationship between the haematocrit and PSBC in our study and this mirrors findings from studies in a CKD population and in participants presenting with cardiac disease requiring surgical treatment [29, 30]. Our finding of a positive relationship between PSBC and albumin agrees with findings by Kraut *et al* [31]. The low oncortic pressure induced by hypoalbuminemia could explain a link between endothelial/ microcirculatory dysfunction and albuminuria because of the multiple roles played by albumin in transport of hormones and other chemical substances in the blood.

We found a positive relationship between the severity of MA and the incidences of IDH. MA suppresses calcium release from the sarcomere in addition to inducing vasodilatation, leading to IDH. The use of non-selective cardio-inhibitory beta adrenergic drugs only act to aggravate the cardiac inhibition [32]. In this study, intradialysis death was more likely to be associated with low SBC than with normal SBC. Kalantar-Zadeh *et al* [33] reported that normal SBC is protective against many adverse consequences of dialysis treatment and ESRD in general.

The positive relationship between the dialysis dose and PSBC in this study mirrors findings that MA was a risk factor for inadequate dialysis [33, 34]. The type of dialysis catheter used impacted on the dialysis dose which is expected to be positively related to the PSBC of the next session. Sessions with AVF and tunneled IJV had higher dialysis doses than non-tunneled and femoral catheters and this mirrors findings by Mutevelic *et al* [35].

In CKD, particularly in ESKD, drugs used in treating these patients could impact on SBC. Loop diuretics and thiazides ameliorate acidosis while potassium sparing diuretics and more so, vasopressin inhibitors (vaptans) inhibit bicarbonate absorption at the distal tubules and collecting duct thereby worsening MA [36]. The use of calcium based phosphate binders can affect SBC, as alkalizing products, calcium carbonate ameliorate acidosis, through buffering H^+ and mitigates the demineralization of bone in MA. However, supranormal and excessive blood calcium could lead to coronary vessel calcification. The 1:1 chloride buffering by bicarbonate further worsens MA and increases the anion gap, typical of ureamia [37]. The use of bicarbonate buffer in place of acetate has reduced the incidence of MA, it is reported that dialysate HCO_3 of 40-42 mmol/L are safe and of benefit in the management of MA [38]. Though we used a dialysate bicarbonate concentration of 34 mmol/L, the fact that it was well above the mean predialysis SBC of a typical dialysis population, even in the developed world, means a reasonable level of blood acid buffering would have been achieved with it.

Limitations

Limitations encountered included non-determination of the residual kidney function and its contribution to the dialysis dose. The dry weight of participants could not be determined. The presence of some co-morbidities/confounders could not be ruled out. Some dialysis intervals were irregular. Dry weight of participants was not determined. Compliance with directives to avoid heavy meals two hours prior to dialysis and adherence to drug use were difficult to ascertain. However, the two centre design and the relative sample size would have contributed to the strength of the study.

Conclusion

The prevalence of MA amongst MHD patients was 79.0%, in a low income setting. Even after dialysis, the prevalence of MA was still high (38.3%). Risk factors for MA included female gender, advancing age, infrequent dialysis and elevated blood pressure, low GFR, use of temporary catheters and dialysis <4 hours.

MA was a risk factor for the occurrence of both IDH and IDHT, dialysis termination, inadequate dialysis and intradialysis death. Metabolic acidosis was associated with hypoalbuminaemia and anaemia. Dialysis delivery should be optimized to meet the KDOQI PSBC target of >22 mmol/L in low income settings which will ultimately improve the dialysis dose in order to reduce the occurrence and complications of MA.

Recommendations

There is the need for greater involvement of governmental, non-governmental agencies and philanthropists in funding dialysis treatment to increase its frequency.

A minimum SBC of 22mmol/l should be taken as the threshold for MA in patients with CKD particularly ESRD to improve their QOL.

Definitions

- Targeted post dialysis weight: Difference between the pre dialysis weight and the UFV plus fluid and blood volume administered. (litres).
- IDH: Systolic blood pressure fall from predialysis value of $\geq$20 mmHg with symptoms.15.
- IDHT: Systolic blood pressure rise from predialysis value >10 mmHg 5.
- Anaemia: PCV <33%. 16
- Hypoalbuminaemia: <35g/dL.17

- In this study, predialysis serum bicarbonate concentration (PSBC) was classified as very low (VL-PSBC), <18.00 mmol/L; low (L-PSBC), 18.00-19.99 mmol/L and normal (N-PSBC), ≥20.0 mmol/L). The adequacy of the dialysis dose was classified as inadequate (Kt/V <1.2 and URR <65.0%) or adequate (Kt/V ≥1.2 and URR ≥65.0%).
- Renal biopsy was not used in classifying the aetiology of CKD in this study, therefore, hypertension associated CKD (HACKD) was defined as long standing hypertension complicated by kidney disease that is commonly found from middle age upwards while CGN was defined as kidney disease leading to hypertension in the young and early middle age with or without history of pharyngitis or skin sepsis in childhood or adolescence.

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Authors' Contributions

Conceptualization and design of paper: PKU; Collection of data: PKU; Data analysis and interpretation: PKU, SOA, FOS, SK; Manuscript drafting: PKU; Manuscript writing: PKU, SOA, FOS, SK; Intellectual critical review: PKU, SOA, FOS, SK; and All authors read and approved the final manuscript before submission.

Conflict of interest

The authors declare no conflict of interest.

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