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ORIGINAL ARTICLE

PATTERN AND PREDICTORS OF INTRADIALYTIC MORTALITY IN AN URBAN DIALYSIS CENTRE IN SOUTH-WEST NIGERIA: A 3-YEAR AUDIT

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ABSTRACT

Introduction

Kidney (renal) replacement therapy is an integral component of the holistic care of patients with renal impairment. It may have adverse outcomes including intradialytic mortality. This study evaluates the prevalence as well as the factors contributing to intradialytic mortality in the studied population.

Methods

A retrospective evaluation of the clinical and dialysis records of 188 adult patients who had haemodialysis in our facility over a 3-year period was performed. A comparison of clinico-demographic parameters was carried out between patients who experienced intradialytic mortality and those who had uneventful dialysis sessions. Data were analysed using SPSS version 24.

Results

During the years under review, 14(7.4%) of the 188 patients dialysed experienced intradialytic mortality with a mean age of 40.6±16.0 years for those that died. More females died intradialysis compared to their male counterparts (M:F ratio = 1:3.6). The source of admission for dialysis (P=0.046), female gender (P=0.05), occurrence of intradialytic hypotension (P=0.001), high predialytic systolic blood pressure (P=0.039), underlying type of kidney disease (P=0.023), intra-dialytic level of consciousness

(P=0.001) as well as dialysis reaction time (P=0.009) were associated with increased likelihood of intra-dialytic death. On multivariate analysis source of admission (OD=0.000, P-value=0.998), in-patient status at last dialysis (OD=0,000, P-value=0.992), intradialytic hypotension (OD=0.000, Pvalue=0.980), predialytic systolic pressure (OD=25.431, P-value=0.981) and reaction time (OD=1696, value=0.981) were not predictive of mortality.

Conclusion

The occurrence of intradialytic mortality is dependent on predialytic as well as intradialytic factors although none of these factors exhibited predictive ability on multivariate analysis.

Keywords: Intradialytic mortality; Haemodialysis; Kidney Replacement Therapy; Chronic Kidney Disease; Acute Kidney Injury

INTRODUCTION

The enormous proportion of kidney impairment-related global disease burden has risen steeply in the past decade with an unfavorable skewness towards the developing economies of which sub-Saharan Africa is a part. This rising trend is worrisome. In the latter part of the last decade, chronic kidney disease (CKD) occupied the 12th position as

the cause of death globally compared to the 17th position it previously occupied three decades ago with an increase in mortality of over 40%.²

Chronic kidney impairment represents a major cause of public health worry world-wide with resultant unfavorable effects on diseases.³ Kidney replacement therapy (KRT) which ranges from various forms of dialysis to kidney transplantation has revolutionised the management of kidney diseases globally irrespective of the type and underlying aetiology of the kidney impairment.4 Haemodialysis, which serves as a stop-gap to kidney transplantation is a globally recognised viable treatment option in patients with end stage kidney disease (ESKD). Despite the respite it brought to the management of kidney diseases, it is still bedeviled with its peculiarities and problems.^{5,6}

a recent survey by Bello et haemodialysis (HD) accounted for nearly 70% of all forms of KRT and almost 90% of all forms of dialysis in the approximately 4 million patients dependent on various forms of KRT globally.⁶ The differences in reported effects of HD world-wide have been linked to the lack of consensus measures of HD effects although efforts are being made, as evidenced by a recent survey involving close to seventywith countries globally five (75)identification of four major HD outcome criteria which must include mortality assessment.⁷

Various complications following the initiation of dialysis have been highlighted both locally and globally in diverse proportions. 4,6,8,9 Reports on death occurring during dialysis are sparse or non-existent, especially in lowincome economies, including Nigeria.^{8,9} The few studies that mentioned mortality only highlighted it as a follow-up tool to analyse the survival or otherwise of patients who had dialysis and were silent on when the deaths occurred.^{8,9} In a recent study carried out in the Northern part of the country, 20(4.4%) out of the 457 patients who underwent HD over a 5vear period experienced death while undergoing dialysis.¹⁰

Diverse works carried out on intradialytic mortality highlighted factors responsible for the death of haemodialysis patients, with some of these factors exhibiting predictive ability although kidney disease patients have a higher propensity for mortality when compared to age- and sex-matched healthy individuals. Advancing age, race, predialytic blood albumin level, predialytic activity status, presence of malignancies and cardiac failure have been linked to the occurrence of intradialytic deaths. 12

Low blood pressure prior to the onset of elevated blood pressure, dialysis, ventricular hypertrophy, hyperlipidaemia, level of awareness before and or during dialysis, increased pulse pressure, diabetes mellitus and poor nutritional status are vital determinants of intradialytic mortality in patients with kidney impairment. 13,14,15,16 Owing to the paucity of data on intradialytic deaths in low-income economies, a retrospective analysis of the clinico-demographic parameters of patients who had intradialytic mortality within the years under review was carried out to elucidate variables linked with its occurrence with the aim of identifying additional measures that can be instituted either pharmacologically or nonpharmacologically to reduce and/or prevent its occurrence.

METHODS

A retrospective evaluation of the clinical records and dialysis charts of 188 patients aged 13 years and above who were offered haemodialysis at the Dialysis Unit of UNIOSUN Teaching Hospital (formerly LAUTECH Teaching Hospital), Osogbo, Nigeria, between March 2019 and February 2022 was done. The study was approved by the Ethics and Research Committee of Osun State University, Osogbo, Osun State, Nigeria. A comparison of the clinico-demographic data between patients who died intradialysis (cases) and those who had uneventful dialysis sessions (control) was undertaken. The cases and control were age-, gender- and diagnosismatched in a ratio of 1:3 using randomly construed numbers.

Bamikefa TA et al - Pattern and predictors of intradialytic mortality in an urban dialysis centre in South-West Nigeria: A 3-year audit

A structured proforma was employed to obtain information relating to demography, source of the referral to dialysis unit, type of kidney impairment, underlying aetiology of kidney disease, precipitant(s) of kidney dysfunction biochemical parameters and commencement of dialysis. Information regarding the level of consciousness prior to and/or during final dialysis, presence/absence of co-morbidities, duration between diagnosis and commencement of initial dialysis (dialysis reaction time), total dialysis sessions given and the interval between initial and final dialysis session (death reaction time) were also recorded. Other information entered were: regularity of dialysis, duration of final dialysis, time and day of demise, intradialytic blood pressure fluctuations during final dialysis, pressure readings before dialysis blood commencement, haematocrit and potassium level before final dialysis as well as time spent during final dialysis.

Statistical Product and Service Solutions (SPSS) version 24 was used for the analysis of the data retrieved. Frequencies and percentages were employed in the presentation of categorical variables, while mean (+standard deviation) or median (interquartile) were used summarise continuous variables applicable. Continuous variables were compared using Student's t-test, while categorical variables were compared using Chi-square. Logistic regression analysis was carried out as appropriate to highlight likely determinants of intradialytic mortality among the study participants with the p-value set at < 0.05.

RESULTS

During the three (3) years under review, 14(7.4%) of the 188 patients dialysed had intradialytic mortality with a mean age of 40.6 ± 16.0 years for those that died. There was a female preponderance among those that died (78.6%) when compared to the male (21.4%) with a male-to-female (M: F) ratio of 1:3.6. The age range of those that died intradialysis was between 13 years to 65 years with more deaths occurring in those between 40-60 years (n=7,50%). A larger proportion of those that died were married (71.4%) while only 28.6%

were unmarried. Seven (50%) of the fourteen (14) patients that had mortality were traders (table 1). More deaths were observed in the year 2020 where 10 (71.4%) patients died compared to the preceding year where four (28.6%) mortalities were recorded. No death was recorded in the year 2021.

Emergency haemodialysis was carried out on all the patients that died. The majority of the deaths occurred in April-June and October-December quarters of 2020 with 5 (35.7%) deaths each. The other deaths were distributed across the months as shown in Table 1. Fifty percent of the deaths occurred in patients admitted through the Accident and Emergency unit of the hospital. It was remotely followed by the female medical ward (14.3%). The other wards contributed 7.1% each. Five (35.7%) patients died during their initiating dialysis session, while the patient that had the highest number of dialysis died during the twenty-seventh session.

Access for HD was through the femoral vein in a large proportion of the patients (n= 13, 93%), with internal jugular cannulation coming a distant second (n=1, 7.1%). Total dialysis sessions were 79, with a mean of 5.6 ± 1.9 sessions. Among those that died, CKD was the commonest diagnosis (n= 8, 57.2%), while acute kidney injury (AKI) in the failure stage accounted for 32.8% of the diagnosis.

The different aetiologies underlying the type of kidney impairment are shown in Table1. The commonest precipitant of AKI was sepsis which accounted for 50%, followed by accelerated hypertension (22%). Nephrotoxins accounted for 14% of the precipitants while the underlying precipitant could not be identified in another 14%.

An equal proportion of patients (35.7%) experienced death less than 2 hours intradialysis and in the last hour into the last dialysis session. More patients were able to do haemodialysis within the first 24 hours of admission (n=6, 42.9%), while only 1(7.1%) patient had dialysis reaction time of 5 days. The median duration on dialysis in those that died was 1.98±0.57 hours.

The interval between initial and terminal dialysis varied between <2 hours in 35.7% and >10 days in 28.6% of patients. A large proportion of the patients (n=11, 78.6%) had irregular dialysis sessions. The majority (n=8, were conscious prior 57.1%) to commencement of dialysis. Intradialytic blood pressure fluctuations ranging from hypotension (n=11, 78.6%) and hypertension (n=2, 14.3%) were observed in the patients (table 2). Half of the deaths occurred on Friday (50%) and mostly at night (n=8, 57.1%). The other clinico-demographic attributes of the patients with intradialytic mortality are shown in Table 1. The baseline attributes of the study population stratified according to outcome are shown in Table 2.

The source of in- hospital patient referral for dialysis (P=0.046), female gender (P=0.05), the occurrence of intradialytic hypotension (P=0.001) and underlying type of kidney disease (P=0.023) were associated with increased likelihood of intra-dialytic death in patients that died when compared to patients that survived. High predialytic systolic blood pressure (P=0.039), intra-dialytic level of consciousness (P=0.001) as well as dialysis reaction time (P=0.009) were other factors that contributed significantly to intradialytic mortality in the studied population. (Table 3)

Elevated blood pressure during dialysis was not statistically linked to an increased occurrence of intradialytic deaths. The mean serum level of potassium at terminal dialysis though higher in those that died during dialysis when compared to the control group was not statistically contributory (P=0.500). On multivariate regression analysis, as shown in Table 4, no factor(s) could be independently associated with the occurrence of intradialytic mortality in the studied population.

Table 1: Clinico-demographic parameters of patient who had intradialytic mortality

of patient who had intradialytic mortality					
Clinical Parameters	Frequency	Percentage			
	(n=14)	(%)			
Gender					
Male	3	21.4			
Female	11	78.6			
Marital Status					
Married	10	71.4			
Single	4	28.0			
Occupation					
Artisan	2	14.3			
Trader	7	50.0			
Retiree/Student	4	28.6			
Civil Servant	1	7.1			
Month of Death					
January-March	3	21.4			
April-June	5	35.7			
July-September	1	7.1			
October-December	5	35.7			
Year of Death					
2019	4	28.6			
2020	10	71.4			
2021	0	0			
Day of Death					
Friday	7	50			
Tuesday	5	35.7			
Wednesday	2	14.3			
Time of Death					
Evening	2	14.3			
Midnight	3	21.4			
Night	8	57.1			
Noon	1	7.1			
Diagnosis					
Chronic kidney Disease	8	57.2			
Acute kidney injury	6	42.8			
Aetiology of CKD					
Glomerulonephritis	4	28.6			
Hypertension	3	21.4			
Obstructive Uropathy	1	7.1			
Aetiology of AKI					
Malignancy	1	7.1			
Sepsis	3	21.4			
Pre-eclampsia	2	14.3			
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AKI- Acute Kidney Injury, CKD-chronic kidney disease

Bamikefa TA $et\ al-Pattern\ and\ predictors\ of\ intradialytic\ mortality\ in\ an\ urban\ dialysis\ centre\ in\ South-West\ Nigeria:\ A\ 3-year\ audit$

Table 2: Baseline characteristics stratified according to outcome

Parameters	Intradialytic	Control	X^2	P-value
	Death n=14 (%)	n=42 (%)		
Gender				
Male	3 (21.4)	27 (64.3)	7.754	0.005^*
Female	11(78.6)	15 (35.7)		
Age (years)				
< 40	6 (42.9)	11 (26.2)		
40-60	7 (50.0)	23 (54.8)	1.885	0.065
> 60	1 (7.1)	8 (19.0)		
Mean Age (yrs)	40.64 ±15.98	49.93 ±15.95	1.931	0.381
Serum K ⁺	4.55 ±1.03	4.26 ±0.91	0.933+	0.356
(mmol/L)				
SerumNa (mmol/L)	131.93 ±7.25	130.57 ±5.45	0.680^{+}	0.500
Serum Urea (mmol)	16.57 ±1.99	17.25±1.86	1.193+	0.254
SerumCreatinine (µmol/l)	1008.21±496.4	1206.97±542.45	1.156+	0.286
Mean initial PCV (%)	24.14±5.17	22.51±7.57	1.794+	0.480
Intradialytic hypotension Yes No	11(78.6)	11(26.2)		
110	3 (21.4)	31 (73.8)	12.07	0.001^*
Intradialytic hypertension				
Yes				
No	2(14.3)	1(2.4)	2.935	0.087
G 641.	12 (87.7)	41(97.6)		
Source of Admission				
A&E	7(50)	16(29.1)		
FMW	7(50)	16(38.1)		
FSW	2(14.3)	6(14.3)	14 210	0.046*
Gynae	1(7.1)	0	14.310	0.046*
ICU	1(7.1)	1(2.4)		
MMW	1(7.1)	1(2.4)		
PNW	1(7.1)	18(42.9)		
D'	1(7.1)	0		
Diagnosis	9(57.2)	20(02.9)	10.240	0.022*
CKD	8(57.2)	39(92.8)	19.248	0.023*
AKI	6 (42.8)	3 (7.2)		

K-Potassium, Na- Sodium, PCV-pack cell volume, A&E- Accident & Emergency, FMW- Female Medical Ward, FSW- Female Surgical Ward, GYNAC- Gynecology Ward, ICU- Intensive Care Unit, MMW- Male Medical Ward, PNW- Post Natal Ward. CKD- Chronic kidney disease, AKI- Acute kidney injury.

^{*} Statistically significant at a P-value of < 0.05. ⁺T-test value

Table 3: Factors associated with intradialytic mortality in the study population

Parameters	Intradialytic	Control	P-value
	Mortality (n=14)	(n=42)	
Last Predialytic SBP (mmHg)	150.50±23.26	N/A	
Last Predialytic DBP (mmHg)	92.50±16.36	N/A	
Predialytic PP (mmHg)	65.36±18.75	71.07±18.03	0.342
Predialytic SBP (mmHg)	155.29±25.81	110.07±78.22	0.039*
Predialytic DBP (mmHg)	89.93±16.18	88.35±15.50	0.758
Awareness level at last dialysis			
Conscious	8 (57.1)	42 (100)	
Lethargic	3 (21.4)	0	0.001^*
Unconscious	3 (21.4)	0	
Dialysis reaction time (Days)	2.36±1.45	1.60 ±0.67	0.009*
Death reaction time (Days)	14.71 ±5.42	N/A	
Last Predialytic PCV (%)	22.50 ± 5.61	N/A	
Duration on dialysis (Days)	11.71±4.41	10.02±1.12	0.596

SBP-Systolic blood pressure, DBP-Diastolic blood pressure, PCV-Packed cell volume, PP- Pulse pressure. * Statistically significant at a P-value of < 0.05.

Table 4: Independent predictor of Intradialytic mortality

PARAMETERS	β VALUE	P-VALUE	ODD'S RATIO
Source of admission	-126.796	0.998	0.000
Awareness level at last dialysis	-302.649	0.992	0.000
Predialytic SBP	3.236	0.981	25.431
Dialysis reaction time	104.144	0.981	1696
Female Gender	61.252	0.990	399
Intradialytic Hypotension	-162.331	0.980	0.000
Diagnosis	449.578	0.995	0.0001
Constant	-525.674	0.994	0.000

SBP- Systolic blood pressure

DISCUSSION

The occurrence of intradialytic mortality in fourteen (14) out of the total one hundred and eighty-eight (188) patients studied put the prevalence of intradialytic death at 7.4% which is higher than the 4.5% reported by Liman et al. 10 in the Northern part of the country. However, both studies were retrospective in nature. The slightly higher prevalence observed in this study might be due to the shorter study duration and fewer patients recruited compared to the study by Liman et al., 10 which was a five (5) year study involving

four hundred and fifty-seven participants. In a previous five-year audit of haemodialysis records carried out in this study centre by Okunola et al., a total of one hundred and thirty-six (136) patients died at various times during treatment follow-up. In another seven-year retrospective study in the Northern part of the country, fifty-six (56) mortalities were reported at different times. However, these findings cannot be compared with that reported in this study since it was not stated that the mortalities were observed intradialysis.

Bamikefa TA et al - Pattern and predictors of intradialytic mortality in an urban dialysis centre in South-West Nigeria: A 3-year audit

In another study carried out in Ethiopia, death in patients offered haemodialysis was reported in 45.1% at various times in and out of the hospital with no specific reference to where the deaths occurred making comparison with this study difficult.¹⁷ In a multi-centered study of 5,774,708 patients on haemodialysis therapy in the United States of America (USA), 31(13%) patients experienced cardiac arrest intradialysis out of the total 400 sudden death documented. 18 This is higher than documented prevalence rate of 7.4% in this study and may be attributed to larger sample size in that study. Majority of the patients who had intradialytic mortality were traders with irregular and/or-limited financial capability, which differs from the observation by Liman et al., 10 where a larger proportion had wellpaying jobs. This finding further corroborates earlier documentation of economic hardship encountered by haemodialysis end users in low-income economies.¹

The occurrence of mortality was higher in when compared to the participants in alignment with the observation in USA although it differs from the higher male preponderance earlier reported in the country and elsewhere in Africa. 10,17,18 The mean age of 40.64±15.98 years seen in this study and the highest proportion of CKD in this study attributable to glomerulonephritis are similar to previously documented findings on dialysis in the country. 8,9,10 This is at variance to the developed and high-income economies where patients on haemodialysis belong to the older age group with CKD commonly due non-communicable to aetiologies. 18,19 The aetiological difference observed has been linked to increased infection-related CKD in the lower-income economies compared to the developed nations.¹⁹ In this study, AKI accounted for 42.8% of the mortality recorded, with sepsis responsible for a large proportion. This is in keeping with the fact that worldwide, CKD contributes a larger proportion of patients to the dialysis pool compared to AKI. 1,8,9

Haemodialysis initiation was on an emergency basis in all the patients in this study, which further confirms the previous finding in this environment. This may be attributed to poor health- seeking attitude, poverty, ignorance and late referral to a nephrologist. 8,9 In a study in Cameroon, the initiation of dialysis was prearranged in 74 out of the 661 (11.2%) patients seen which is at variance to the observation in this study.20 More mortalities occurred on Friday (50%), closely followed by Tuesday (35.7%), which is close to the finding by Liman et al., 10 where most deaths occurred on Friday and Wednesday and at variance with the finding in the USA where more deaths were observed on Monday and Wednesday.¹⁸ The reason for increased mortality in the midnight observed in this study could not be fully explained but may be due to a lack of a full complement of personnel during call hours, although equal occurrence between daytime and night has been reported in the country. 10

Mortality was frequently encountered within the first hour into dialysis in the dialysis naïve patients whose first session usually last 2 hours in our centre as well as the last hour of dialysis for patients with prior dialysis exposure. In this study, more deaths were recorded during the first dialysis session (35.7%). In the study in the northern part of the country, majority of the deaths were recorded after about 2 hours on dialysis,. The timing of intradialytic mortalities in this study, compares favorably with earlier findings in developed countries. 18

In the mortalities reported in this study, dialysis was carried out via temporary double lumen femoral catheter in 93% (13 patients) compared to tunneled jugular catheter in 7% (1 patient), which is at variance with the findings in Ethiopia and the USA where other access types had a higher percentage. 17,18 The use of temporary catheters as access for dialysis was the most statistically significant mortality (P< 0.0001) determinant in a retrospective study done in Ethiopia.¹⁷ The predominant utilisation of temporary femoral catheters in this study may be due to the poor clinical state of the patient at presentation making it difficult for a neck line to be sited. Late referral for nephrologist assessment, emergency presentation, high cost of dialysis care and low nephrologist-patient ratio in our centre among other factors may be responsible for the predominant use of temporary vascular access for dialysis in our centre.

The survivors were older than those that had mortality in this study. This conflicts with earlier reports in this country and beyond. This may be linked to the underlying aetiology of CKD in this study which has been reported to be commoner in younger age group. the lower age in hence deceased. 8,10,15,18 The source of in-hospital transfer for nephrologist intervention and the level of patient's awareness prior to dialysis was significantly associated with intradialytic mortalities. Fluctuations in the level of consciousness and the need for dialysis in patients with end-organ damage have been associated with an increased likelihood of mortality.²¹ Although low haematocrit level has been linked with adverse outcomes in patients with CKD; it did not statistically contribute to mortality in this study despite the low level in both the deceased and the control groups.8,9,22

There was no statistically significant variation in the blood sodium, urea, potassium and creatinine level between the deceased and the controls. The mean serum creatinine in both groups was in keeping with findings in other climes. 17, 23 Although high blood level of been shown has potassium arrhythmogenic often with fatal outcome, it did not exhibit statistically significant link with intradialytic mortality despite its elevation in this study.²⁴ High predialytic systolic blood pressure (p=0.039) was statistically associated with intradialytic mortality in this study which is in keeping with earlier findings that extremes of blood pressure prior to and/or during dialysis will affect dialysis outcome negatively and sometimes lead to death. 13,25 In study the dialysis reaction time significantly contributed to mortality during dialysis although this is at variance to earlier report of its non-significant contribution to death during dialysis in Nigeria.¹⁰

On multivariate analysis, the effect of clinicodemographic factors on intradialytic mortality could not be further corroborated owing probably to low number of patients in both arms of the study making the observed variation to be undetected. Although low serum albumin, abnormal lipid level, poor nutritional status and left ventricular thickening are important determinants of death in patient on haemodialysis, evaluation for these factors could not be carried out because of the retrospective study design as well as incomplete and/or missing data. 14,15,25

CONCLUSION

The likelihood of death during dialysis is higher in the female young/middle age patients, emergency presentation, impaired level of awareness at dialysis initiation, presence of blood pressure fluctuation prior and/or during dialysis initiation as well as in patients with chronic kidney disease irrespective of the underlying cause. Measures to reduce the occurrence of intradialytic hypotension, effective pre- & intradialytic blood pressure control, early referral to nephrologist to allow for planned dialysis and arteriovenous fistula (AVF) creation and cardiovascular risk assessment proper routine including intra-dialytic electrocardiogram (ECG) in patients with high cardiovascular risks must be carried out in patients requiring kidney replacement therapy irrespective of the type and underlying cause of kidney (renal) impairment.

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Bamikefa TA et al - Pattern and predictors of intradialytic mortality in an urban dialysis centre in South-West Nigeria: A 3-year audit

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