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Determinants of Adequacy of Haemodialysis among End-Stage Renal Disease Patients on Maintenance Haemodialysis at General Hospital Calabar: A Retrospective Study

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Abstract: End-stage renal disease (ESRD) is an irreversible condition where patient's survival is dependent on renal replacement therapy (RRT). Haemodialysis (HD) is a modality of RRT that is used in the treatment of patients with ESRD who cannot afford or are awaiting renal transplantation. This study, therefore, aims at determining factors associated with the adequacy of HD in ESRD patients on maintenance HD. A retrospective study that reviewed medical records of all the ESRD patients who were on maintenance HD at the dialysis unit of the General Hospital, Calabar (GHC) in Southern Nigeria. A total of 54 patients were reviewed but only 50 patients had complete data for analysis. Socio-demographic, clinical and biochemical data were obtained from the records in the dialysis unit and calculated Kt/V was used to assess the adequacy of HD.There were more males 29 (58.0%) than females 21 (42.0%) in the study. The mean age was 51.71±15.43 years and 43.04±14.03 years for males and females respectively. Inadequate HD measured using Kt/V and urea reduction ratio (URR) occurred in 76.0% and 80.0% of the study population respectively. Factors associated with adequate HD were use of high flux dialyzer, longer duration of HD, higher blood flow rate (BFR), higher ultrafiltration (UF) Goal, increased number of HD sessions per week, higher post-dialysis estimated glomerular filtration rate (eGFR) and lower post-dialysis urea. In the logistic regression model analysis, the predictors of adequacy of dialysis (Kt/V) were the use of high flux dialyzer (OR- 1.190-22.222, $p = 0.028$), increased number of HD sessions per week (OR- 0.011-0.589, $p = 0.013$), lower post-dialysis urea (OR- 0.365-0.791, $p = 0.002$) and post-dialysis creatinine levels (OR- 1.000-1.009, $p = 0.029$). Our study shows that the major determinants of the adequacy of HD are the use of high flux dialyzer and an increased number of HD sessions per week and these may have influenced the post-dialysis urea and creatinine levels.

Key words: Adequacy · End-Stage Renal Disease · Determinants · Haemodialysis

INTRODUCTION

End-stage renal disease (ESRD) is an irreversible condition for which patient's survival is dependent on renal replacement therapy (RRT) [1].

Haemodialysis (HD) is a modality of renal replacement therapy (RRT) that is used in the treatment of patients with chronic kidney disease especially those with ESRD who cannot afford or awaiting renal transplantation [2]. In these patients, long term morbidity and mortality

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outcomes have been demonstrated to be dependent on the adequacy of dialysis dose [3].

Adequacy of dialysis refers to dialysis that enables patients to have a normal quality of life (QOL) with good clinical tolerance and minimal problems during the dialysis and interdialytic periods [4].

Studies have shown that dialysis is inadequate in most of the patients with ESRD receiving HD and the factors associated with the inadequacy are late presentation, shorter duration and reduced frequency of dialysis sessions, uremic bleeding, septicemia, repeated blood transfusions and low-functioning vascular access [5, 6].

Dialysis adequacy can be determined clinically and by related biochemical and mathematically derived formulae which have been shown to correlate with patients' outcomes [7].

These include Urea Reduction Ratio (URR) which is a measure of the adequacy of the delivered dose of dialysis expressed as a percentage reduction in blood urea level after a session of dialysis. It is mathematically related to Kt/V and both can be derived from each other with some amount of precision by various equations or a normogram [8].

Although Kt/V is the recommended measure of dialysis adequacy, but URR is mainly utilized because of its simplicity and similar predictive power to Kt/V in terms of patient's outcome [9, 10]. A URR of 65% which corresponds with Kt/V of 1.2 is the minimum acceptable dose in the standard thrice weekly haemodialysis [8, 11]. Studies have documented a mean urea reduction ratio (URR) of 41.83% [5] and an inadequate HD dose in 60 % [6] in the various study populations respectively.

The few available reports in our environment showed that dialysis was inadequate in most patients and patients' survival was poor. Furthermore, most of these studies mainly utilized the URR to determine adequacy of dialysis without calculating or utilizing the dialysis machine online Kt/V values [5, 12, 13].

Our study intends to determine the factors associated with adequate haemodialysis among ESRD patients on maintenance HD with the use of calculated Kt/V values at the dialysis unit of the General Hospital, Calabar.

MATERIALS AND METHODS

A retrospective study that reviewed medical records of all the ESRD patients who were on maintenance haemodialysis at the dialysis unit of the General Hospital, Calabar (GHC) for a two-year period from January 2014 to December 2016. A total of 54 patients were reviewed but only 50 patients had complete data for analysis.

Information regarding the patient's demography, blood pressure measurements using an automated machine attached to the dialysis bed, laboratory investigations and haemodialysis prescriptions were obtained from the dialysis records and entered into a data template.

The blood flow rate for the dialysis sessions was between 150 to 350mls/min with a dialysate flow rate of 500mls/min for all patients. The pre and post dialysis blood samples were taken at each HD session. Predialysis blood sample was taken before commencement of each dialysis session.

In patients with vascular access catheter in-situ, 5mls of blood sample was initially taken from the arterial catheter and discarded before another 5mls syringe was used to take sample for estimation of pre-dialysis blood urea nitrogen to avoid the dilution effect of saline and heparin.

At the end of each dialysis session, the dialysate flow was shut off for 3 minutes while the blood flow went at full tilt. The blood sample for post-dialysis urea estimation was taken about 3 minutes after dialysis from the arterial sampling port to negate the effect of access recirculation.

The urea reduction ratio (URR) for three consecutive haemodialysis sessions were calculated for each patient using this formula:

$$[1 - U_{post} / U_{pre}] \times 100$$

where Upre=predialysis blood urea concentration and Upost=post dialysis blood urea concentration and average of the values obtained [10].

Also, the Kt/V values for three consecutive HD sessions were calculated using the second generation Daugirdas formula: [8] and average obtained.

$$\text{Single pool Kt/V} = -\text{In}\,(R - 0.008 \times t) + (4 - 3.5 \times R) \times \text{UF/W}$$

where In represents the natural logarithm, R is the ratio of post dialysis to predialysis BUN, t is the length of a dialysis session in hours, UF is the ultrafiltration volume in liters and W is the patient's post dialysis weight in kilograms.

Data Analysis: The data obtained was analysed using Statistical Package For Social Sciences (SPSS) version 18. Continuous variables and categorical variables were expressed as means ±S.D and percentages respectively. Independent sample t-test, Chi-square test, ANOVA and other statistical tests were used as appropriate. $P < 0.05$ was considered to be significant.

RESULTS

Table 1 showed that the mean age for females and males were 42.67±9.75 years and 48.72±13.65 years respectively. The mean Kt/V was 0.86±0.32 while mean URR was 49.94±12.98% and the commonest aetiology of ESRD was chronic glomerulonephritis (36.0%) which is closely followed by diabetic nephropathy (34.0%). The commonest vascular access was through the femoral vein (66.0%) while low flux dialyzer (54.0%) was commonly used by the participants. Haemodialysis was inadequate in 76.0% and 80.0% of participants using the Kt/v and URR respectively.

Table 2 showed that longer duration of haemodialysis, higher UF goal, increased number of haemodialysis sessions per week, lower levels of post-dialysis urea and the use of high flux dialyzer were associated with adequate haemodialysis ($p< 0.05$).

Table 3 showed that the duration of haemodialysis, BFR, UF Goal, number of haemodialysis sessions per week and post-dialysis eGFR were positively correlated while post-dialysis urea was negatively correlated with Kt/v.

Multiple linear regression model in Table 4 showed that the predictors of adequacy of dialysis were higher number of haemodialysis sessions per week, higher pre-dialysis urea and lower post-dialysis urea levels.

In this logistic regression model in Table 5, the variables that were predictors of adequacy of haemodialysis are the use of high flux dialyzer, increased number of haemodialysis sessions per week, lower post-dialysis urea and post-dialysis creatinine levels.

Table 1: Demographic and Clinical Parameters of Participants

Variables	Frequency (%), Mean±SD
Age (years)	
Female	42.67±9.75
Male	48.72±13.65, p= 0.073
Gender	
Female	21(42.0)
Male	29(58.0)
Aetiology of CKD	
HTN	7(14.0)
DM	17(34.0)
CGN	18(36.0)
Obstructive Nephropathy	1(2.0)
HIVAN	7(14.0)
Vascular Access	
Femoral	33(66.0)
Internal Jugular	15(30.0)
Arteriovenous Fistula	2(14.0)
Type of Dialyzer	
Low Flux	27(54.0)
High Flux	23(46.0)
Kt/v	0.86±0.32
Urea Reduction Ratio (%)	49.94±12.98
Kt/V Category	
< 1.2	38(76.0)
≥ 1.2	12(24.0)
Urea Reduction Ratio	
< 65%	40(80.0)
≥ 65%	10(20.0)

CKD-Chronic kidney disease, HTN-Hypertension, DM-Diabetes mellitus, CGN-Chronic glomerulonephritis, HIVAN-Human immunodeficiency virus associated nephropathy

Table 2: Relationship of Kt/v with Clinical and Biochemical Parameters

Variables	(N=38) Kt/V < 1.2, (%)	(N=12) Kt/V ≥ 1.2, (%)	P - value
Age (years)	46.58±13.20	44.92±9.90	0.645
Pre-dialysis weight (kg)	77.58±11.23	79.92±7.42	0.413
Duration of haemodialysis (hours)	3.13±0.70	3.67±0.49	0.007*
BFR (mls/min)	315.0±44.22	341.67±63.37	0.195
UF Goal (litres)	2.04±1.12	3.04±0.72	0.001*
Sessions of haemodialysis /week	1.68±0.66	2.42±0.67	0.004*
Pre-DSBP	160.68±27.35	176.33±26.75	0.095
Pre-DDBP	91.63±15.32	101.75±12.28	0.029*
Pre-dialysis PCV (%)	24.5±4.06	27.0±5.41	0.161
Pre-dialysis urea (mmol/l)	31.77±7.73	30.13±6.22	0.461
Pre-dialysis creatinine (µmol/l)	1025.57±563.46	1070.03±672.33	0.838
Post-dialysis urea (mmol/l)	17.78±5.48	11.0±3.02	0.001*
Post-dialysis creatinine (µmol/l)	652.69±456.04	538.86±262.4	0.289
Post-dialysis eGFR (mls/min)	19.06±14.67	21.59±15.67	0.626
Type of vascular access			
Femoral	28(73.7%)	5(41.9%)	0.130
Internal Jugular	9(23.7%)	6(50.0%)	
Arteriovenous Fistula	1(2.6)	1(8.3%)	
Type of dialyzer			
Low flux	24(63.2%)	3(25.0%)	0.021*
High flux	14(36.8%)	9(75.0%)	

BFR- Blood flow rate, UF-Ultrafiltration, DSBP-Dialysis systolic blood pressure, DDBP-Dialysis diastolic blood pressure, PCV-Packed cell volume
*Significant p-value

Table 3: Correlation to Determine the Factors Associated with Adequacy (Kt/v) of Haemodialysis

Variables	Correlation coefficient	p-value
Age (years)	-0.064	0.660
Predialysis weight(kg)	0.200	0.164
Duration of dialysis (hours)	0.531**	0.0001
BFR (mls/min)	0.313*	0.027
UF Goal (litres)	0.521**	0.0001
Sessions of haemodialysis/week	0.452**	0.001
Pre-DSBP	0.230	0.108
Pre-DDBP	0.211	0.140
Pre-dialysis PCV (%)	0.215	0.134
Pre-dialysis urea (mmol/l)	-0.149	0.301
Pre-dialysis creatinine (µmol/l)	-0.121	0.403
Post-dialysis urea (mmol/l)	-0.741*	0.0001
Post-dialysis creatinine (µmol/l)	-0.260	0.069
Post-dialysis eGFR (mls/min)	0.341*	0.015

BFR-Blood flow rate, UF-Ultrafiltration, DSBP-Dialysis systolic blood pressure, DDBP-Dialysis diastolic blood pressure, PCV-Packed cell volume
**correlation is significant at the 0.01 level (2- tailed)
*correlation is significant at the 0.05 level (2- tailed)

Table 4: Multiple Linear Regression for Predictors of Adequacy (Kt/v) of Haemodialysis

Variables	Beta	t	P - value
Predialysis weight (kg)	-0.091	-1.121	0.270
Duration of haemodialysis (hours)	0.133	1.666	0.105
BFR (mls/min)	0.040	0.454	0.652
UF Goal (litres)	0.164	1.540	0.133
Sessions of haemodialysis /week	0.218	2.448	0.020*
Pre-DSBP	0.020	0.224	0.824
Pre-DDBP	-0.101	-0.924	0.362
Pre-dialysis PCV (%)	0.019	0.233	0.817
Pre-dialysis urea (mmol/l)	0.431	3.716	0.001*
Pre-dialysis creatinine (µmol/l)	-0.034	-0.234	0.817
Post-dialysis urea (mmol/l)	-1.030	-8.478	0.0001*
Post-dialysis creatinine (µmol/l)	0.279	1.696	0.099
Post-dialysis eGFR (mls/min)	0.069	0.600	0.552

BFR-Blood flow rate, UF-Ultrafiltration, DSBP-Dialysis systolic blood pressure, DDBP-Dialysis diastolic blood pressure, PCV-Packed
*Significant p-value

Table 5: Logistic Regression Analysis for the Predictors of Adequacy (Kt/v) of Haemodialysis

Variables	Exp. B	95% CI/Odds ratio	p-value
Age	1.044	0.946-1.153	0.393
Gender (1)	1.018	0.273-3.796	0.919
Type of vascular access(1)	5.600	0.299-104.931	0.249
Type of vascular access(2)	1.500	0.078-28.890	0.788
Type of dialyzer (1)	5.143	1.190-22.222	0.028*
Pre-dialysis weight (kg)	1.033	0.923-1.156	0.572
Duration of haemodialysis (hours)	0.222	0.031-1.615	0.137
BFR (mls/min)	0.999	0.977-1.022	0.943
UF Goal (litres)	0.458	0.158-1.327	0.150
Sessions of haemodialysis /week	0.680	0.011-0.589	0.013*
Pre-dialysis urea (mmol/l)	0.928	0.813-1.060	0.271
Pre-dialysis creatinine (µmol/l)	1.001	0.999-1.002	0.347
Post-dialysis urea (mmol/l)	0.537	0.365-0.791	0.002*
Post-dialysis creatinine (µmol/l)	1.005	1.000-1.009	0.029*
Post-dialysis eGFR (mls/min)	0.990	0.949-1.033	0.645

BFR-Blood flow rate, eGFR-Estimated glomerular filtration rate, UF-Ultrafiltration,
*Significant p-value

DISCUSSION

In most studies, adequate haemodialysis (HD) is largely dependent on the delivered dose of HD as measured by Kt/V [6, 14].

A mean Kt/V of 0.86±0.32 and URR of 49.94±12.98% were obtained in this study and these findings are in agreement with similar studies in Nigeria and other developing countries. [5, 6, 13]. The two studies earlier mentioned in Nigeria had mean URR values of 41.8% and 45.3% respectively without Kt/V values; the study in Nepal had URR of 65.3% with Kt/V of 0.99 while about 60% of a study population in Egypt had Kt/V < 1.2 [5, 6, 13, 15].

Despite the better URR value amongst Nepalese patients as compared to our study, the Kt/V values in Nepal and Egypt still demonstrated inadequate haemodialysis [6, 15]. This shows that Kt/V is a better representation of adequacy of haemodialysis because of the correction for ultrafiltration and urea generation as shown in Daugirdas formula (8). Our study showed that URR is strongly correlated with Kt/V, which is similar to findings in other studies [6, 16].

Data from the National Cooperative Dialysis Study showed that Kt/V < 0.8 was associated with a high morbidity, while a better outcome was seen in patients with Kt/V values between 1.0 and 1.2 [3]. However, our study did not assess the morbidity and outcome as these parameters were not available in this retrospective study. In addition, patients may have dialysed for only a few months.

In our study, the factors that appear to have contributed to adequate HD are the use of high flux dialyzer, longer duration of HD, higher BFR, higher UF goal increased number of HD sessions per week, higher post-dialysis eGFR and lower post-dialysis urea.

Interestingly, on further analysis, the factors that were found to be associated with adequacy of dialysis (Kt/V) after correcting for confounding factors are the use of high flux dialyzer, increased number of haemodialysis sessions per week, lower post-dialysis urea and post-dialysis creatinine levels.

In this study, increased BFR is associated with adequacy of HD as this was statistically significant and in agreement with some studies. It is important to note that those studies related the BFR to the clearance rate of solutes, where a better clearance rate was associated with a better Kt/V [6, 17].

As regards the frequency and duration of HD session, we found that increased frequency and longer duration of HD were associated with better Kt/V and these findings are in keeping with reports from some studies [6, 18]. Also, the prescription of a higher UF goal has shown to be associated with improvement in the Kt/V values as demonstrated in this present study which is in agreement with findings from a related study [6].

In our study, the use of high flux dialyzer was associated with adequacy of HD as compared to use of low flux dialyzer. The high flux dialyzers used in our environment are dialyzers with larger surface area and studies have shown that dialyzers with larger surface area give better solute clearance rates of urea. They also permit the removal of middle and higher molecular weight solutes during dialysis [19, 20]. High flux dialyzers are more expensive compared with the low flux ones. However, the cost of dialysis was subsidized by nearly 50% at GHC enabling patients' access to the dialyzers.

Patients with adequate HD are expected to have a better clearance of solutes such as urea and creatinine. To a reasonable extent, the clearance rate is dependent on the dialyzer surface area as shown in earlier studies [19, 20]. It may not be surprising therefore that our study showed lower post-dialysis urea, creatinine and higher post-dialysis eGFR to be associated with improved Kt/V.

CONCLUSION

Our study showed that inadequate haemodialysis is not uncommon in our environment and the major determinants of adequacy of HD are the use of high flux dialyzers and increased number of haemodialysis sessions per week.

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Limitations of the Study: In view of the retrospective nature of this study and presence of missing data for analysis, non inclusion of important parameters such as clearance rates and vascular access recirculation, making a conclusion on the predictors of adequacy of HD may not be complete.

Secondly, the calculated Kt/V value which is a measure of adequacy of HD was not used to determine patient's outcome as most patients could not continue with dialysis due to financial constraints while some others were lost to follow up.

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