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Prevalence and Predictors of Hemodialysis Inadequacy among Patients on Maintenance Hemodialysis in Mwanza, Tanzania

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Abstract

Introduction: The burden of chronic kidney disease (CKD) is rapidly increasing in Tanzania. There is a rapid expansion of hemodialysis (HD) services to meet this demand. The quality of HD services, which is usually termed HD inadequacy, is under-reported. Therefore, the objective of this study was to determine the prevalence of HD inadequacy using two equations, urea reduction ratio (URR) and Kt/V and its associated factors. The correlation between URR and Kt/V for the diagnosis of HD inadequacy is also determined. **Materials and Methods:** This was a prospective longitudinal study conducted from March to July 2021 in 98 patients with CKD who underwent maintenance HD at Bugando Medical Centre in Mwanza, Tanzania. Demographic, laboratory, and clinical information was collected and analyzed. The HD inadequacy was estimated by using both the URR and the Kt/V equations. The correlation between the two equations was analyzed by using Cohen's kappa. **Results:** The majority (69.4%) of the study participants were male and the mean age was 59 (48 - 68) years. The median hemoglobin level was 10 (8.9 - 11.2) g/dl, and the pre-dialytic urea was 15 (10.6 - 21.3) mmol/L. The prevalence of HD inadequacy was 36 (36.7%). The predictors of HD inadequacy were older age (>50 years) (OR = 3.6, 95 % CI 1.0 - 12.6, p = 0.04), moderate or severe anemia (OR = 4.7, 95 % CI 1.5 - 14.4, p = 0.006) and short duration of HD (OR = 3.1, 95 % CI 1.0 - 9.1, p = 0.04). There was a strong agreement between URR and Kt/V in the diagnosis of HD inadequacy (Kappa = 0.887). **Conclusion and Recommendations:** HD inadequacy is common, and most predictors can be prevented. Clinicians should use a personalized approach in making sure that anemia is appropriately treated and HD prescription is adhered to for better clinical outcomes among patients with HD.

Keywords

Hemodialysis Inadequacy, Prevalence, Tanzania, URR, Kt/V

1. Introduction

Chronic kidney disease (CKD) is one of the leading causes of morbidity and mortality worldwide. It is a global health burden with high economic costs for health systems [1] The prevalence of CKD in the general population of the African continent is 15.8% and is higher in countries of sub-Saharan Africa (SSA) than in the rest of the continent [2] In Tanzania, the prevalence of CKD ranges from 7% to 15% in the general population and 27.5% to 83.7% in hospital studies [3].

Kidney transplantation (KT) remains the main treatment option with better treatment outcomes for CKD patients. Because of its high cost and inaccessibility to most CKD patients, particularly in those in resource-constrained settings like Tanzania, maintenance hemodialysis (HD) is the most commonly used modality for renal replacement therapy. HD when performed efficiently has been shown to improve quality of life and reduce mortality [1] [3]. Efficient HD is usually determined by HD adequacy which is a measure of urea clearance in the body. The most efficient and recommended methods to estimate HD adequacy are the urea reduction ratio (URR) and Kt/V (K: clearance of urea, T: duration of HD session and V: volume of urea distribution). The cut-offs for adequate dialysis are 65% and 1.2 for URR and Kt/V, respectively. URR is calculated as follows:

$$\frac{\text{Pre-dialysis urea} - \text{post-dialysis urea}}{(\text{Pre-dialytic urea}) \times 100\%} \quad [4]$$

HD inadequacy is one of the major problems of successful HD and has been associated with increased mortality and morbidity. According to a recent review, 31% of people on maintenance HD therapy in SSA countries died, and most of these deaths were related to suboptimal dialysis quality [5]. In Tanzania, the mortality among patients on maintenance HD is reported to be 17% [6]. Although many developing countries rarely assess and report HD adequacy parameters [5] [7] [8], few available studies show a high prevalence of dialysis inadequacy; Iran (63.7%), Egypt (67%), Sri Lanka (78.8%), India (78%) and Rwanda (38%) [9] [10] compared to developed countries where the prevalence is less than 10% in North America, Western Europe, and Australia [11]. There is scarcity of data on the quality of dialysis offered in Tanzania, the study by Somji *et al.* [12] reported prevalence of 65.7% using URR and 59.4% using Kt/V among patients who were on maintenance HD in multiple centers in the city of Dar es Salaam. As of 2018, there were about 30 functioning HD centers in Tanzania

[13], however, the country is currently rapidly expanding HD services to reach about 8500 people who are in need countrywide [14]. Expansion of HD services should be matched with the desirable quality of such services, raising an urgent need to establish the efficacy of such services in the country. Furthermore, despite the global recommendations of URR and Kt/V as the key indicators for assessing HD adequacy, their usefulness and consistency in the local settings have to be explored towards improving patient outcomes. The main aim of this study was to determine the prevalence and predictors of HD inadequacy among patients undergoing maintenance hemodialysis in Mwanza, Tanzania and to assess the similarities between URR and Kt/V equations in the diagnosis of HD inadequacy.

2. Material and Methods

Study design and setting

This was a prospective longitudinal study conducted from March to July 2021 at the HD Ward of Bugando Medical Center (BMC), Mwanza Region. BMC is a consultant and university teaching hospital located in northwest Tanzania which serves a population of approximately 13 million people, with a bed capacity of 1300. The HD unit at BMC was set up in July 2016 and has 21 working machines, a total of 104 patients with CKD are receiving maintenance HD at BMC. About 50 patients are said to visit the department daily, with each patient coming in for treatment three times a week.

Data collection

Serial screening was performed on all 104 patients. Clinical and demographic data were collected through interview and from clinical notes by an investigator after obtaining written informed consent and explaining the purpose of the study to participants. These included age, gender, marital status, educational level, place of residence, number of HD sessions per week, type of vascular access, and comorbidities. Pre-, intra- and post-dialytic examinations were performed according to the hospital's HD protocol. In addition, blood samples for urea were drawn from the arterial line before and after dialysis of each patient to calculate URR and Kt/V according to standard guidelines [18]. Corresponding blood pressure (BP) values were also measured, and mean blood pressure values were referred to as pre-dialytic blood pressure or post-dialytic blood pressure. The standard pre-tested questionnaire that was designed by the investigator based on the research objectives was used to collect these data. Validity of this tool was tested by using the content validity method.

Definitions

Hemodialysis inadequacy was defined as inadequate removal of toxins and waste products from the patient's blood which had a negative impact on their quality of life and was determined by URR < 65% and/or Kt/V < 1.2 [12].

Data analysis

Data was entered into Excel database and analyzed using STATA version 13.

Descriptive statistics were used to summarize demographic and clinical characteristics; continuous variables were reported as medians with interquartile ranges (IQR) and discrete variables were reported as frequencies and proportions and compared using chi-square test. Predictors of HD inadequacy were determined using logistic regression, with all variables with a p-value < 0.2 in univariate analysis being subjected to multivariate analysis and those with a p-value < 0.05 were considered to be statistically significant. The goodness of fit for the final model was then evaluated. The sensitivity and specificity of independent factors in the final model were assessed to determine their discriminating ability. The Receiver Operating Characteristic (ROC) curves were used according to the Hanley and McNeil's method to determine the cut points with the best sensitivity and specificity. The correlation between URR and Kt/V values was summarized in the scatterplot of Pearson's correlation coefficient (R), where an R of 0.5 to 1.0 was considered large association strength and a p-value < 0.05 was considered to be significant. The mismatch of diagnosis of HD inadequacy between URR and Kt/V was measured by using Cohen's kappa (K), where K = 0.8 to 0.9 was considered to be strong and K > 0.9 was almost perfect.

Ethical clearance

Permission to conduct this study was granted by the Joint Ethics Committee of the Bugando Medical Centre/Catholic University of Health and Allied Sciences with accession number CREC/462/2021 and written informed consent was obtained from all participants.

3. Results

Characteristics and demographics of the study participants

A total of 104 patients were recruited, of whom 98 were included in the study. Six patients were excluded for multiple reasons; 3 were lost to follow up, 2 refused to consent and 1 was under 18 years old. Of the 98 patients who were enrolled into the study, 69.4% were male and the mean age was 59 years (IQR 48 - 68 years). The median BMI was 22.9 (IQR 20.6 - 25.9) kg/m^2. The majority (84.7%) of the patients had hypertension, of which 52/83 (62.6%) had only hypertension, 33/83 (33.6%) had diabetes mellitus and 31/83 (37.3%) had both hypertension and diabetes. The median hemoglobin (Hb) was 10 (IQR 8.9 - 11.2) g/dl, pre-dialytic urea was 15 (IQR 10.6 - 21.3) mmol/L and eGFR was 8 (IQR 6 - 11) ml/min/1.73m^2. The median duration of HD was 7 (IQR 4 - 25) months with at least three sessions per week and the most frequently used access was semi-permanent catheters in 60 (61.2%) patients (Table 1).

Prevalence of Hemodialysis inadequacy

Of the 98 participants, HD was found to be inadequate in 36/98 (36.7%) when using Kt/V and 31 (31.6%) when using URR. The prevalence of HD inadequacy by URR or Kt/V was 36 (36.7%).

Clinical profile of CKD patients by hemodialysis outcomes

Patients with HD inadequacy were more likely to be elderly (33.3% vs 16.1%,

Table 1. Baseline and clinical characteristics of the study population (n = 98).

Variable	Frequency (%) or Median (IQR)
Age (years)	59 (48 - 68)
18 - 40	15 (15.3)
41 - 50	16 (16.3)
51 - 60	22 (22.4)
>60	45 (45.9)
Sex	
Male	68 (69.4)
Female	30 (30.6)
Education level	
None	7 (7.1)
Primary	42 (42.9)
Secondary	13 (13.3)
College or above	36 (36.7)
Body Mass Index (Kg/m^2)	22.9 (20.6 - 25.9)
Underlying disease	
Hypertension	52 (53.1)
Diabetes	33 (33.6)
Hypertension and Diabetes	31 (31.6)
HIV	5 (5.1)
Pre-dialytic SBP (mmHg)	151 (133 - 171)
Pre-dialytic DBP (mmHg)	81 (68 - 90)
Pre-dialytic Blood Urea Nitrogen (mmol/L)	15 (10.6 - 21.3)
Pre-dialytic eGFR (mls/min/1.73m^2) * (n = 90)	8 (6 - 11)
Hemoglobin (g/dl)	10 (8.9 - 11.2)
Serum Albumin (g/dl)	3.8 (2.6 - 4.2)
Duration on hemodialysis (months)	7 (4 - 25)
Frequency of hemodialysis sessions per week	3 (3 - 3)
Dialyzer surface area (m^2)	1.6 (1.4 - 1.8)
Blood flow rate (mls/min)	300 (250 - 300)
Ultrafiltration (mls)	1730 ± 102)
Type of access	
Semi-permanent	60 (61.2)
Arterio-venous fistula	22 (22.5)
Temporary vascular access	16 (16.3)
URR (%)	68.6 (61.3 - 75.6)
Kt/V	1.2 (0.9 - 1.4)

IQR: Interquartile range.

p = 0.04), have HIV infection (11.1% vs 1.6%, p = 0.04), and had short-term duration of HD (<7 months) (63.9% vs 40.3%, p = 0.02) compared to those with adequate HD. Patients with obesity (38.9% vs 22.5%), elevated pre-dialytic SBP (77.8% vs 59.7%), severe anemia(25.0% vs 11.3%) and high blood flow rate (BFR) (22.2% vs 8.1%) comprised majority of those with HD inadequacy, but the differences were not statistically significant (p > 0.05 for all) (Table 2).

Table 2. Demographic and clinical profile of study patients by hemodialysis outcomes (n = 98).

Variable	Hemodialysis Inadequacy Proportion (%) or Median IQR) (n = 36)	Hemodialysis Adequacy Proportion (%) or Median IQR) (n = 62)	p-value
Age (years)			
18 - 40	3 (8.3)	12 (19.3)	0.14
41 - 50	4 (11.1)	12 (19.3)	0.29
51 - 60	12 (33.3)	10 (16.1)	**0.04**
>60	17 (47.2)	28 (45.1)	0.84
Sex			0.38
Male	13 (36.1)	17 (27.4)	
Female	23 (63.9)	45 (72.6)	
Education level			0.09
Primary or none	14 (38.9)	22 (61.1)	
Secondary or above	27 (43.5)	35 (56.4)	
Body Mass Index (Kg/m^2)			
<18.5 (Underweight)	1 (2.8)	5 (8.1)	0.29
18.5 - 24.9 (Normal)	21 (58.3)	43 (69.4)	0.27
25 - 29.9 (Overweight)	6 (16.7)	9 (14.5)	0.78
≥30 (Obese)	14 (38.9)	14 (22.5)	0.08
Underlying disease			
Hypertension	18 (50.0)	34 (54.8)	0.64
Diabetes	10 (27.8)	21 (33.9)	0.53
HIV	4 (11.1)	1 (1.6)	**0.04**
Pre-dialytic blood pressure (mmHg)			0.07
SBP ≥ 140	28 (77.8)	37 (59.7)	
SBP < 140)	8 (22.2)	25 (40.3)	
Pre-dialytic blood pressure (mmHg)			0.36
DBP ≥ 90	13 (36.1)	16 (25.8)	
DBP < 90	23 (63.9)	46 (74.2)	
Pre-dialytic blood urea nitrogen			0.65

Continued

Normal (<8.5 mmol/L)	4 (11.1)	5 (8.1)	
High (≥8.5 mmol/L)	32 (88.9)	57 (91.9)	
CKD stage by eGFR (mls/min/1.73m^2)*			
Stage 4 (16 - 29)	6 (19.3)	8 (13.8)	0.61
Stage 5 (<16)	25 (80.6)	50 (86.2)	0.21
Hemoglobin (g/dl)			
Normal (>12 in female or 13 in males)	2 (5.6)	9 (14.5)	0.18
Mild Anemia10 -12 or 13	9 (25.0)	26 (41.9)	0.09
Moderate Anemia (8 -10)	16 (44.4)	20 (32.3)	0.23
Severe/life threatening anemia (<8)	9 (25.0)	7 (11.3)	0.08
Serum albumin (g/dl)			0.59
Normal (>3.4)	28 (77.8)	51 (82.3)	
Low (≤3.4)	8 (22.2)	11 (17.7)	
Duration on hemodialysis (months)			**0.02**
<7 months	23 (63.9)	25 (40.3)	
≥7 months	13 (36.1)	37 (59.7)	
Frequency of hemodialysis sessions per week			0.08
3 times	34 (94.4)	51 (82.3)	
<3 times	2 (5.6)	11 (17.7)	
Dialyzer surface area (m^2)			0.32
≥1.6	16 (44.4)	34 (54.8)	
<1.6	20 (55.6)	28 (45.2)	
Blood flow rate (mls/min)			0.05
>300	8 (22.2)	5 (8.1)	
≤300	28 (77.8)	39 (62.9)	
Type of access			
Semi-permanent	37 (59.7)	23 (63.9)	0.83
Arterio-venous fistula	16 (25.8)	6 (16.7)	0.33
Temporary vascular access	9 (14.5)	7 (19.4)	0.58

*9 participants are missing due to incomplete results. IQR: Interquartile range; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; CKD: Chronic kidney disease; eGFR: Estimated glomerular filtration rate.

Predictors of hemodialysis inadequacy

Using multivariate logistic regression, older age >50 years [3.6 (1.0 - 12.6, p = 0.04), moderate or severe anemia [(2.9 (1.2 - 2.7), p = 0.006] and short duration of hemodialysis (<7 months) [2.6 (1.1 - 6.1), p = 0.04]) were found to be strong predictors of HD inadequacy. A positive correlation was observed between HD inadequacy with elevated pre-dialytic SBP [3.5 (1.1 - 11.3), p = 0.05], and high BFR [3.7 (0.9 - 14.9), p = 0.07], but it was not statistically significant (Table 3).

The Hosmer-Lemeshow goodness-of-fit test showed no apparent lack of fit, with an area under the ROC curve of 0.80 (p = 0.20) (Figure 1).

Agreement of URR and Kt/V in the diagnosis of HD inadequacy

The URR and Kt/V equations agreed in 100% (n = 31) and 92.5% (n = 62) for the diagnosis of HD inadequacy and HD adequacy, respectively. Only 7.5% (n = 5) had conflicting results of URR and Kt/V. In general, this agreement was strong with Kappa (K) = 0.887) (Table 4).

A scatterplot of the Pearson's correlation coefficient (R) between URR and Kt/V values is shown in Figure 2, where there is a significant positive correlation between URR and Kt/V values with an R of 0.926 (p < 0.001).

4. Discussion

In this study, we have determined that more than one third (36.7%) of patients with ESRD receiving maintenance HD in Mwanza, Tanzania, were poorly dialyzed and there was a strong agreement between URR and Kt/V in the diagnosis

Table 3. Predictors of hemodialysis inadequacy.

Variable	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Advanced age (>50 years)	2.6 (0.9 - 6.9)	**0.05**	3.6 (1.0 - 12.6)	**0.04**
Male Sex	1.4 (0.6 - 3.6)	0.37		
Low education level	2. 0 (0.9 - 4.7)	**0.09**	2.6 (0.9 - 7.6)	0.08
Overweight	1.2 (0.4 - 3.6)	0.78		
Obesity	2.2 (0.9 - 5.3)	**0.09**	2.2 (0.7 - 7.1)	0.20
Elevated pre-dialytic SBP	2.4 (0.9 - 6.0)	**0.07**	3.5 (1.1 - 11.3)	0.05
Elevated pre-dialytic DBP	1.6 (0.7 - 3.9)	**0.28**		
Moderate or severe anemia	2.9 (1.2 - 7.0)	**0.01**	4.7 (1.5 - 14.4)	**0.006**
Elevated blood urea nitrogen	1.4 (0.4 - 5.7)	0.62		
Short duration of HD (<7 month)	2.6 (1.1 - 6.1)	**0.03**	3.1 (1.0 - 9.1)	**0.04**
Hypoalbuminemia	1.3 (0.5 - 3.7)	0.59		
Frequency of HD sessions per week	3.7 (0.8 - 17.6)	**0.10**	1.6 (0.2 - 10.5)	0.59
Dialyzer surface area	1.5 (0.7 - 3.5)	0.32		
Blood flow rate > 300	3.2 (0.9 - 10.9)	**0.05**	3.7 (0.9 - 14.9)	0.07
Catheter type				
Temporary	1.3 (0.4 - 4.2)	0.58		
Permanent	1.2 (0.5 - 2.9)	0.65		
Arterio-venous fistula	0.6 (0.2 - 1.7)	0.31		

OR: Odds ratio; CI: Confidence interval.

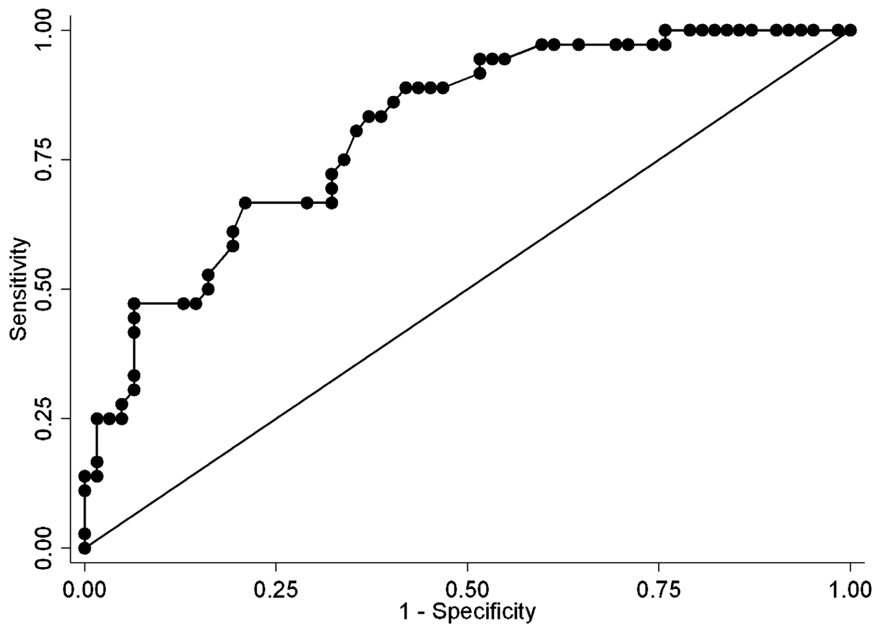

Figure 1. Test for goodness of fit for multivariate logistic model for inadequate dialysis by URR.

Table 4. Agreement of URR and Kt/V.

		URR		Total
		HD adequacy	HD Inadequacy	
Kt/V	HD adequacy	62 (92.5)	0	62
	HD inadequacy	5 (7.5)	31 (100)	36
	Total	67	31	**98**

Kappa = 0.887.

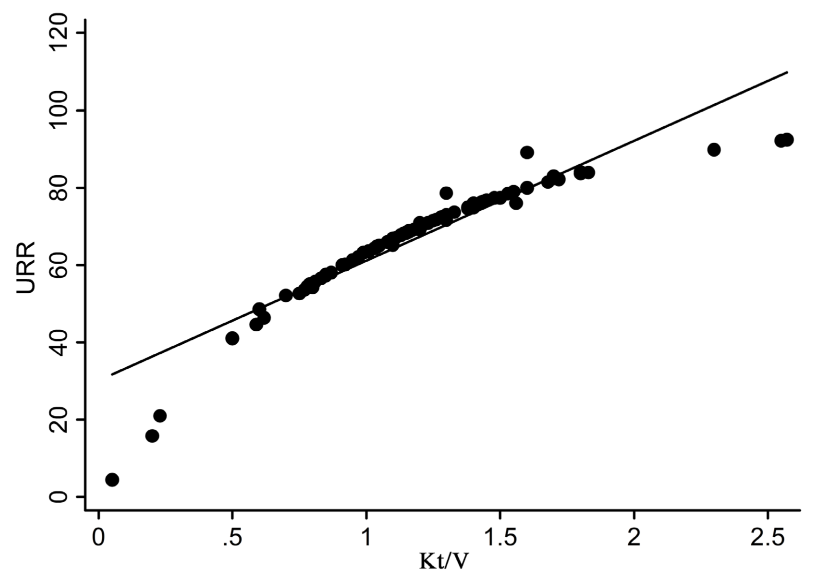

Figure 2. Scatter plot for Pearson's correlation between URR and Kt/V.

of HD inadequacy. The prevalence of HD inadequacy found in this study is almost similar to that reported in Rwanda where 38% of patients received suboptimal hemodialysis [10]. Higher prevalence has been previously documented from other developing countries; India 82% [15], Sri Lanka 82% [16] and Iran 64% [17]. In Tanzania to date there is only one study that was conducted in Dar es Salaam that reported the prevalence of 59.4% and 65.7% by using Kt/V and URR equations, respectively, among 143 participants from four of the largest dialysis centers [12]. The lower prevalence found in our study could be explained by the use of a relatively higher blood flow rate (BFR) (average 300 mL/min) compared to previous studies. A high BFR is correlated with effective HD and is recommended by recent guidelines [18]. It is ascertained that an increase of BFR by 25% results in a significant increase in HD adequacy [17].

Inadequate HD was strongly predicted by advanced age, anemia, and short duration of dialysis. In the index study, we have found that the elderly population had more than two times higher risk of having inadequate HD. These findings complement previous reports from Iran [19] and Rwanda [10] where there was a significant negative correlation between age and inadequate HD. Also, in Tanzania the same findings were previously reported where the older population of 40 years or older comprised the majority of patients with inadequate HD [12]. On the contrary, a study from Palestine [20] did not find this relationship. Frailty and protein-energy malnutrition that are common in aged patients undergoing HD decrease the clearance of dialysis urea and are postulated to be causes of inadequate HD in this group [21]. This particular finding underscores that older adults should be considered for more individualized treatment plans to achieve better results.

Anemia is common among patients with CKD who undergo HD and poor outcomes have been reported among these patients and its effects tend to increase with increasing severity [22] [23]. Our study has found that the vast majority (87%) of the participants were anemic with Hb < 13 g/l in men and Hb < 12 g/l in women. These findings confirm previous study from Tanzania, which reported a high prevalence of 69% among patients undergoing HD [24]. Furthermore, in this study, we have also found that moderate and severe anemia (Hb < 10 g/L) strongly predicted suboptimal dialysis, which is similar to what was reported in previous studies [12]. Taken together, these results underscore the importance of strict adherence to the recommended treatment guidelines for anemia among patients undergoing HD that recommend maintaining hemoglobin between 10 to 12 g/dl for effective HD, and effective HD is an efficient modulator of the anemic process and an adjunct to its treatment [4] [25].

In this study, a short HD duration of less than 7 months showed a strong prediction of suboptimal HD. Similar findings have been previously reported [26]. Several other studies reported that ineffective HD during the first days is common and can lead to multiple complications with adverse outcomes [27], and in turn, the longer duration of HD is correlated with better dialysis outcomes such as anemia correction, fluid status control, minerals metabolism, and patient-reported outcomes [11]. Contrary to these results, a study that was previously conducted in Tanzania didn't show any association between HD inadequacy and duration of HD [12]. This discrepancy could be explained by the type of patients who were recruited. Most (63%) of our patients were on HD for less than 3 months, while all patients included in the Dar es Salaam study were on HD for 3 months or more. Therefore, close monitoring of CKD patients is needed, especially during the early days of HD with individualized therapy.

The prevalence of HD inadequacy in the index study was 36.7% using Kt/V and 31.6% using URR and by URR or Kt/V the prevalence was 36.7%. Generally, Kt/V is considered to be superior to URR in estimating HD adequacy because the latter equation does not account for the effects of ultrafiltration on urea removal and does not account for the effect of urea generation during dialysis. Also, URR is relatively easy to calculate compared to Kt/V since only pre-dialytic and post-dialytic BUN levels are needed [4]. To our knowledge, this is the first study to report on the similarity of Kt/V and URR in the diagnosis of HD inadequacy in the African population. Therefore, our findings that show a strong agreement between two equations should encourage practitioners to intensify the frequency of assessing and reporting HD adequacy/inadequacy parameters by using one of the equations which is appropriate to the local environment.

A major limitation of this study was that we had only 98 patients and it was conducted in one center only. Despite these limitations, the results of our study add to the current body of literature on HD inadequacy.

5. Conclusion

HD inadequacy is common, and most predictors can be prevented. Clinicians should use a personalized approach in making sure that anemia is appropriately treated and HD prescription is adhered to for better clinical outcomes among patients with HD. Also, clinicians should intensify the frequency of assessing and reporting the quality of HD by using either URR or Kt/V or both since all equations are suitable.

Conflicts of Interest

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

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