ORIGINAL RESEARCH ARTICLE

Comorbidity and Haemodialysis Adequacy in End-Stage Kidney Disease Patients in Lesotho

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Keywords: Comorbidity, Mortality, End-stage kidney disease, Adequacy, Haemodialysis, Ureareduction ratio

ABSTRACT

Background: Low- and middle-income countries including Lesotho are faced with a huge burden of end-stage kidney disease in people experiencing human immune virus (HIV), hypertension (HTN) and diabetes mellitus (DM).

Objectives: To assess the comorbidity, mortality rate and evaluate the haemodialysis adequacy in patients with end-stage kidney disease in Motebang government hospital.

Methods: A retrospective study was conducted in 142 adult male and female patients enrolled for haemodialysis from 1st October 2017 to 30th June 2023 in Motebang government hospital. Patient's characteristics and clinical outcomes data were analysed using descriptive statistics

Results: Among 142 patients enrolled, there were 84 (59.2%) males and 58 (40.8%) females. 19 (13.4%) patients were below 34 years while 33 (23.3%) patients were between 45 and 64 years. In all age groups, 41 (28.9%) patients had HIV, 37 (26.1%) patients had HTN alone and 24 (16.9%) patients had combination of HTN and DM. In 63 deceased patients, there were 36 (57.1%) males and 27 (42.7%) females. Among deceased, 18 (28.5%) patients had HIV, 15 (23.8%) had combination of HTN and DM, 14 (22.3%) patients had HTN alone, while all the patients (99.3%) were also anaemic. Since 2017, 19 (30.2%) patients died in 2020, 12 (19%) died in 2022 while only 4 (6.3%) patients died up to date (June 2023). Among 79 patients, only 1 (1.3%) patient had urea-reduction ratio (URR) greater than 65%.

Conclusions: Chronic diseases are the major risks factors in patients with end-stage kidney disease in Motebang hospital. Haemodialysis adequacy should form the integral part of monitoring in patients with end-stage kidney disease to prolong life.

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What do we already know about this topic?
End- stage kidney disease (ESKD) is a serious health problem in lower and middle income countries.
What is the main contribution to Evidence-Based Practice from this article?
The major leading risk factors to the prognosis of end-stage kidney disease especially in older people in Lesotho include HIV, HTN and DM. All the end-stage kidney disease in Motebang government hospital had anaemia.
What are this research's implications towards health policy?
Different strategies for screening, early diagnosis and good management of these comorbidities at primary healthcare level should be strengthened to limit progression to ESKD. Urea-reduction-ratio in patients with ESKD should be conducted routinely as the part of the blood monitoring of biomarkers such as serum haemoglobin, urea, and creatinine.

Authors' Contributions Statement:
PP- contributed to planning of the study, supervised the study, and obtained ethical approval; assist in collection of data, performed the statistical analysis of the study, wrote-up the first draft of the manuscript and prepare the manuscript for submission. BL- wrote up the proposal for the study, prepared it for ethics approval, undertook the, collected the data and proof-read the final manuscript. RM- assist in the data collection, data interpretation and proof-read the final manuscript. LM- assisted with the statistical analysis, data interpretation and proof-

Introduction

End- stage kidney disease (ESKD) is a serious health problem in lower and middle income countries. The Kidney Disease Improving Global Outcomes (KDIGO) CKD work group defined ESKD as anabnormalities of a kidney structure or function, present for more than three months with impactions for health, characterised by estimated Glomerular filtration rate (e-GFR) of less than 15 ml/min/1.73m^2 for at least three months (Kidney Disease, 2023). According to the Global Disease Burden (GBD) on renal system report of 1990-2017, ESKD has emerged as a leading cause of global mortality in this era (GBD Chronic Kidney Disease Collaboration, 2020). Epidemiological studies estimated that ESKD affects over 10% of the global population amounting to over 800 million individuals (Kovesdy CP, 2022; Rhee C & Kovesdy C, 2015). In 2010, it was estimated that, around 2.6 million ESKD patients all over the world have once enrolled in haemodialysis and a two-fold increase is expected by 2030 (Sartika KD & Sunaka IW,2022). Four studies showed that Human Immune Virus (HIV), hypertension (HTN), and diabetes mellitus (DM) are the major global comorbidities leading to ESKD (Webster AC et al., 2017; Mallappallil M et al., 2014; Damtie S et al., 2018; Rayner BL et al., 2023). The World Health Organisation (WHO) 1990-2013 survey study and Lesotho Population-Based HIV Impact Assessment (LePHIA) 2016-2017 report demonstrated that Lesotho is among the countries highly affected by various disease burden, with the prevalence of 31% HTN, 25% HIV, and 1.3% DM of the total population (World Health Organization, 2018& PHIA Project, 2018). The GBD renal system report of 1990-2017 revealed that in Lesotho, number of deaths due to ESKD were 417 (338 to 501) (GBD Chronic Kidney Disease Collaboration, 2020).

The ESKD should be diagnosed early, monitored and the patient's comorbidities should be treated. The routine clinical monitoring of blood biochemical markers for ESKD include urea, blood-urea-nitrogen (BUN), creatinine and haemoglobin (Higgins C, 2016). The application of pharmacokinetics method of kidney performance and adequacy clearance measure (urea-reduction-ratio) of haemodialysis in patients with ESKD have been implemented worldwide (Sartika KD & Sunaka

IW, 2022; Liang KV et al., 2019; Nisha R et al., 2017). (Higgins C, 2016) suggested that the importance for the evaluation of creatinine, urea or BUN is that these biomarkers can reflect the GFR. Creatinine monitoring is one of the simpler method of evaluating changes to the kidney function in patients with ESKD (Elendu Cet al., 2023). Creatinine is a waste product produced from muscle mass metabolism and commonly used to estimate the e-GFR in patients with ESKD (Elendu Cet al., 2023). Previous studies have showed that creatinine monitoring in patients with ESKD is of paramount in the monitoring of prognosis of the diseases since the biomarker concentration increases with a decrease in GFR, aging and increased muscle mass (Higgins C,2016; Liang KV et al.,2019; Nisha R et al.,2017).

The Kidney Disease Outcome Initiative (KDOQI) guidelines showed that haemodialysis can improve patient's health outcomes in long-term use (Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines, 2006). Previous studies revealed that high mortality in patients with ESKD are associated with high levels of creatinine, urea and BUN (Higgins C, 2016; Liang KV et al., 2019). Although serum urea is not recommended for regular evaluation of kidney function due to lack of specificity (Higgins C, 2016), however, the urea levels before and after haemodialysis are used in the calculation of urea-reduction-ration (URR), one of the most commonly used parameter to evaluate the adequacy of haemodialysis in patients with acute kidney injury (Liang KV et al., 2019) and ESKD (Sartika KD & Sunaka IW, 2022; Chijioke A et al., 2009). The KDOQI guidelines recommends that URR greater than 65% (URR > 65%) reflect adequate haemolysis and well controlled urea levels in patients with ESKD (Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines, 2006). Sartika and Sunaka revealed that URR >65% is associated with improved quality of life in patients with ESKD (Sartika KD & Sunaka IW, 2022). Screening patients for ESKD, proper management of comorbidities and monitoring of URR should be done routinely in both in-patients and out-patients in all health facilities. Previous study in Motebang government hospital had focused on the challenges to adherence to management and barriers that result in non-adherence to dialysis sessions (Chitja M et al., 2021). Although some comorbidities were noted in the study, review was conducted from 1st October 2017 to 31st December 2018 which lacked recent morbidity and mortality data as well as measurement of haemodialysis adequacy in patients with ESKD (Chitja M et al., 2021). To date, the haemodialysis adequacy in patients with ESKD remains unknown, therefore, this study aimed to assess the comorbidity, mortality and evaluate haemodialysis adequacy in patient with ESKD in Motebang government hospital in Lesotho.

Methods

Study design and study settings

A cross-sectional retrospective study was conducted using patient files review in 142 adult patients (including deceased and active patients) diagnosed with end–stage kidney failure. The study was conducted in Motebang government hospital renal unit located in Hlotse, Leribe. Due to a limited number of patients enrolled in the haemodialysis centre, the inclusion criteria were all male and female adult patients, within the age range of 18 to 70 years, enrolled for haemodialysis for more than 3 months (received at least 1 dialysis treatment per 3 sessions in a week) from the opening of the renal unit centre in 1st October 2017 to

30th June 2023. A designed and validated data collection tool was used to extract the patient demographic information, comorbidities, mortality and clinical parameters such as serum creatinine, urea, BUN and haemoglobin. For anonymity and confidentiality, the patients were allocated serial numbers linking them to the files for record keeping. The study was approved by the National University of Lesotho International Review Board (NUL-IRB) and Ministry of Health Research Ethics Committee (MOH-REC) (ID 78-2022). Informed consent was not given to the patients since the study was retrospective and only patients files were used to obtain the data, nevertheless, confidentiality was ensured throughout the study.

Data analysis

The patient's data were captured on Microsoft 365 Excel® and patient's demographic data which were categorical variables were analysed with descriptive statistics and presented as percentages per total while the continuous variables were presented as a mean ± standard deviation (SD) and/or median and interquartile range (IQR) based on normality distribution. The Grubbs' test was used to identify any outlier from the given data sets and the Shapiro-Wilk test was used to test for normality of distribution. The Mann-Whitney U (for data not normally distributed) or unpaired t-test with Welch's correction (for normal distributed data) were used to compare relation between two data sets, with the two-tailed statistical significance accepted as $p < 0.05$. The pre- and post-serum urea level, BUN level, creatinine level and urea-reduction-ratio (URR) for 79 patients (excluding 63 deceased patients) for the first 6 months of dialysis until 30th June 2023 were calculated according to described formulas by Higgins and Liang et al.(Higgins C,2016; Liang KV et al., 2019). The URR were presented as percentage of total in a table and on a scatter diagram. The graphs were generated with Microsoft Excel office window 10 and GraphPad Prism (GraphPad software, version 8, San Diego, USA).

Results

Different comorbidities were studied in 142 dialysis patient at Motebang hospital since the commencement of the renal unit on the 1 st October 2017 to the 30th June 2023 (Table 1). The results showed that more males (59.2%, n=84) compared to females (40.8%, n=58) had received dialysis between October 2017 to June 2023. Based on the age groups, 33 (23.2 %) patients aged 45-54 years and 33 (23.2%) patients aged 55-64 years were mostly on dialysis, followed by 31(21.8%) patients aged 35-44 years, and 26 (18.3%) patients aged 65 years and above, while 19 (3.4%) patients were aged between 25-34 years (Table 1). Also, 41 (28.9%) patients had HIV, 37 (26.1%) patients had HTN, 24 (16.9%) patients had HTN and DM, 21 (14.8%) patients had HTN and HIV, 12 (8.5%) patients had HTN, DM and HIV, while 7(4.9%) patients had DM (Table 1). Of note, all the patients were anaemic while 18 (12.7%) patients had additional diseases such as congestive cardiac failure, tuberculosis, bacterial respiratory tract infections, urinary obstruction, benign hyperplasia, coronary artery disease and hypothyroidism (Table 1).

Table 1.

Age group (in years)	25-34		35-44	45-54	55-64	65+	Total %
Gender (% per total)	M	9(6.3)	21(14.8)	20(14.1)	18(12.7)	16(11.3)	84(59.2)
	F	10(7)	10(7)	13(9.2)	15(10.7)	10(7)	58(40.8)
Total % by age		19(13.4)	31(21.8)	33(23.2)	33(23.2)	26(18.3)	142(100)
Comorbidity (%) (n=142)							
HTN	1(0.7)		7(4.9)	9(6.3)	6(4.2)	14(9.9)	37(26.1)
DM	0		1(0.7)	2(1.4)	2(1.4)	2(1.4)	7(4.9)
HIV	10(7)		14(9.9)	13(9.2)	2.1(3)	1(0.7)	41(28.9)
HTN-DM	1(0.7)		1(0.7)	3(2.1)	12(8.5)	7(4.9)	24(16.9)
HTN-DM-HIV	1(0.7)		2(1.4)	2(1.4)	6(4.2)	1(0.7)	12(8.5)
HTN-HIV	6(4.2)		6(4.2)	2.8(4)	4(2.8)	1(0.7)	21(14.8)
Anaemia (, Hb (g/dl))	19(13.4) 8.100 ± 2.146		31(21.8) 8.203± 2.001	33(23.2) 8.894 ± 1.802	33(23.2) 9.415 ± 2.428	26(18.3) 9.715 ± 2.085	142(100)
Others*	1(0.7)		5(3.5)	6(4.2)	3(2.1)	3(2.1)	18(12.7)

Different comorbidities compared by age and gender in 142 dialysis patients in Motebang hospital
Others* (include congestive cardiac failure, tuberculosis, coronary artery disease, hypothyroidism; n-total number of patients; M-Male; F- Female; HTN-Hypertension; DM-Diabetes mellitus; HIV-Human immune virus; HTN-DM- Hypertension-diabetes mellitus; HTN-DM-HIV- Hypertension-Diabetes mellitus- Human immune virus; HTN-HIV-Hypertension-Human immune virus; Hb- Haemoglobin; g/dl-grams per deciliter

Table 2 showed that death was higher in male patients (57.1%, n =36) compared to female patients (42.7%, n=27) from the beginning of the renal unit centre in Motebang hospital. Also, more males aged 35-44 years, 45-54 years and 65+ years died (27.7%, 15.9% and 11.7%) compared to females of the same age groups (6.3%, 4.8% and 3.1%). In deceased patients, HIV was the leading comorbidity found in 18 (28.5%) patients followed by combination of HTN and DM present in 15 (23.8%) patients, HTN alone observed in 14 patients (22.3%), combination of HTN and HIV present in 10 (16%) patients,combination of HIV, DM and HTN observed in 5 (7.9%) patients while DM alone was the least comorbidity with 1 (1.6%) patient (Table 2). Out of 63 patients who died, 63 (99.8%) were anaemic while 3 (4.8 %) patients had other related diseases such as such as congestive cardiac failure and tuberculosis (Table 2). The occurrence of death was higher in 2020 (30.2%, n=19), followed by 12 (19.0%) patients in 2019, 10 (15.9%) patients in 2022, and with 4 (6.3%) patients in 2023 (30th June 2023)

Table 2.Different comorbidities and mortality compared by age and gender in 63 deceased dialysis patients in Motebang hospital

Age group (in years)	25-34		35-44	45-54	55-64	65+	Total %
Gender (%)	M	4(6.3)	8(12.7)	10(15.9)	7(11.1)	7(11.1)	36(57.1)
	F	6(9.5)	4(6.3)	3(4.8)	12(19)	2(3.1)	27(42.7)
Total %		10(15.9)	12(19)	13(20.6)	19(30.2)	9(14.3)	63(100)
Comorbidity (%) (n =63)							
HTN		1(1.6)	3(4.8)	4(6.3)	3(4.8)	3(4.8)	14(22.3)
DM		0	0	1(1.6)	0	0	1(1.6)
HIV		5(7.9)	6(9.5)	4(6.3)	2(3.2)	1.6(1)	18(28.5)
HTN-DM		1(1.6)	1(1.6)	0	14.3(9)	4(6.3)	15(23.8)
HTN-DM-HIV		0	0	1(1.6)	4(6.3)	0	5(7.9)
HTN-HIV		3(4.8)	2(3.2)	3(4.8)	2(3.2)	0	16(10)
Anaemia (Hb (g/dl))		15.8(10) 7.430 ± 1.884	19(12)7 .433± 2.451	22.2(14) 8.146 ±1.665	28.6(18) 8.779± 2.359	14.2(9) 9.067± 2.149	63(99.8)
Others*		0	1(1.6)	2(3.2)	0	0	3(4.8)
Mortality (%)(n=63)							
2017	M	1(1.6)	0	0	0	0	1(1.6)
	F	0	0	0	0	0	
2018	M	0	0	1(1.6)	2(3.2)	2(3.2)	9(14.3)
	F	1(1.6)	1(1.6)	0	1(1.6)	1(1.6)	
2019	M	0	1(1.6)	4(6.3)	1(1.6)	1(1.6)	12(19)
	F	1(1.6)	1(1.6)	1(1.6)	1(1.6)	1(1.6)	
2020	M	1(1.6)	3(4.8)	1(1.6)	2(3.2)	2(3.2)	19(30.2)
	F	1(1.6)	0	3(4.8)	2(3.2)	4(6.3)	
2021	M	1(1.6)	1(1.6)	1(1.6)	0	2(3.2)	8(12.7)
	F	0	1(1.6)	0	2(3.2)	0	
2022	M	0	0	3(4.8)	1(1.6)	0	10(15.9)
	F	2(3.2)	1(1.6)	1(1.6)	2(3.2)	0	
2023	M	0	1(1.6)	1(1.6)	1(1.6)	1(1.6)	4(6.3)
	F	0	0	0	0	0	

M-Male; F-Female; Hb-Haemoglobin hypothyroidism; n- total number of patients; M-Male; F-Female;HTN-Hypertension; DM-Diabetes mellitus; HIV-Human immune virus; HTN-DM- Hypertension-diabetes mellitus; HTN-DM-HIV- Hypertension-Diabetes mellitus- Human immune virus; HTN-HIV-Hypertension-Human immune virus; Hb- Haemoglobin; g/dl-grams per deciliter

Biochemical biomarkers (serum urea, BUN and creatinine) and URR monitoring in 79 dialysis patients (excluding 63 deceased patients) for the first 6 months of starting haemodialysis
The median values of pre- and post- serum urea levels in 79 dialysis patients (excluding 63 deceased) were compared separately in five age groups as shown in Table 3. There was a statistically significant difference between pre and post urea levels in all the age groups (U-test values = 0, 3.5, 0, 0 and 16 in the age 25-34 years, 35-44 years, 45-54 years, 55-64 years and 65 and above years, respectively, with $p < 0.0001$ in all age groups). There was statistically significant difference in the median values of urea in all groups before the haemodialysis compared with the reference range (20-40 mg/dl). The median values of urea levels before haemodialysis were significantly high at 97.8 (88.80-141.3) mg/dl in the 131 age group 25-34 years, 121.2 (84.45-147.2) mg/dl in the age group 35-44 years, 121(110.4-146.4) mg/dl in the age group 45-54 years, 98.40 (90.15-131.6) mg/dl in the age group 55-64 and 113.1(98.70-133.7) mg/dl in the age 65 years and above compared to the post-haemodialysis median values of urea levels at 31.80 (18.00-49.80) mg/dl in the age group 25-34 years, 33.90 (23.10-53.10) mg/dl in the age group 35-44 years, 40.80 (28.20-44.40) in the age group 45-54 years, 30 (23.40-47.25) mg/dl in the age group 55-64 and 39.60 (25.35-51.00) mg/dl in the age 65 years and above (Table 3).

Table 3.Distribution of serum urea in 79 patients on haemodialysis

Serum urea concentration (mg/dl)							
				Pre-haemodialysis	**Post-haemodialysis**		
Age group (in years)	No. of patients	Gender		Median (IQR)	Median (IQR)	*U*- value	P-value
		M	F				
25-34	10	6	4	97.8(88.80-141.3)	31.80(18.00-49.80)	0	0.0001
35-44	24	11	13	121.2(84.45-147.2)	33.90(23.10-53.10)	3.5	0.0001
45-54	17	10	7	121(110.4-146.4)	40.80(28.20-44.40)	0	0.0001
55-64	12	8	4	98.40(90.15-131.6)	30(23.40-47.25)	0	0.0001
65+	16	9	7	113.1(98.70-133.7)	39.60(25.35-51.00)	16	0.0001
(Data are presented as Median (IQR-Interquartile range; n- Number of subjects; M-Male; F- Female; U-value- Mann-Whitney test value; P ≤ 0.05 significant-Statistical significance)							

Comparison of the median values of pre- and post- serum BUN levels in 79 dialysis patients (excluding 63 deceased) in five age groups is shown in Table 4. There was a statistically significant difference in the median BUN levels before and after haemodialysis in all the age groups (U-test values = 0, 3.5, 0,0 and 16 in the age 25-34 years, 35-44 years, 45-54 years, 55-64 years and 65 and above years, respectively, with $p < 0.0001$ in all age groups). There was statistically significant difference in the median values of BUN in all groups before haemodialysis compared with the reference range (7-20mg/dl). There are significantly high median values of BUN levels before dialysis at 45.66 (41.46-65.97)mg/dl in the age group 25-

34 years, 56.58 (39.43-68.70) mg/dl in the age group 35-44 years, 56.86 (51.54-68.35) in the age group 45-54 years, 47.34 (43.21-68.07) mg/dl in the age group 55-64, and 52.80 (46.08-62.39) mg/dl in the age 65 years and above compared to the post haemodialysis median values of BUN levels at 14.85 (8.403-23.25) mg/dl in the age group 25-34 years, 15.83 (10.78-24.7) mg/dl in the age group 35-44 years, 19.05 (13.17-20.73) in the age group 45-54 years, 14.01 (10.92-22.06) mg/dl in the age group 55-64 and 18.49 (11.83-23.81) mg/dl in the age 65 years and above) (Table 4).

Table 4. Distribution of serum BUN in 79 dialysis patients on haemodialysis

Serum BUN concentration (mg/dl)							
				Pre-haemodialysis	**Post-haemodialysis**		
Age group (in years)	No. of patients	Gender		Median (IQR)	Median (IQR)	*U*- value	P-value
		M	F				
25-34	10	6	4	45.66(41.46-65.97)	14.85(8.403-23.25)	0	0.0001
35-44	24	11	13	56.58(39.43-68.70)	15.83(10.78-24.7)	3.5	0.0001
45-54	17	10	7	56.86(51.54-68.35)	19.05(13.17-20.73)	0	0.0001
55-64	12	8	4	47.34 (43.21-68.07)	14.01(10.92-22.06)	0	0.0001
65+	16	9	7	52.80 (46.08-62.39)	18.49(11.83-23.81)	16	0.0001
(Data are presented as Median (IQR-Interquartile range; n- Number of subjects; M-Male; F- Female; U-value- Mann-Whitney test value; P ≤ 0.05 significant-Statistical significance)							

The mean SD values of pre- and post-serum creatinine (in mg/dl) were compared separately in five age groups (Table 5). In all the age groups, there were statistically significant difference ($p < 0.0001$) in serum creatinine before and after haemodialysis sessions (Table 5). The serum creatinine mean values were significantly higher than normal (up to 1.4 mg/dl) in the five age groups ($p <0.0001$). The mean SD values of serum creatinine before haemodialysis in all the age groups were significantly higher ($p < 0.0001$): 8.823 ± 2.520 mg/dl in the age group 25-34 years, 10.92 ± 3.577 mg/dl in the age group 35-44 years, 11.35 ± 2.708 mg/dl in the age group 45-54 years, 9.096 ± 2.172 mg/dl in the age group 55-64, and 10.03 ± 2.109 mg/dl in the age 65 years and above when compared to the mean SD values of after haemodialysis at 3.044 ± 1.083 mg/dl in the age group 25-34 years, 4.263 ± 1.806 mg/dl in the age group 35-44 years, 4.419 ± 1.445 mg/dl in the age group 45-54 years, 9.096 ± 2.172 mg/dl in the age group 55-64, and 4.334 ± 1.978 mg/dl in the age 65 years and above (Table 5). The unpaired t-test shows a statistically significant difference in mean SD before and after haemodialysis in all age groups (t-test = 6.321, 8.412, 9.314, 7.440 and 7.875 in the age 25-34 years, 35-44 years, 45-54 years,55-64 years and 65 and above years, respectively) (Table 5).

Table 5. Distribution of serum creatinine in 79 dialysis patients on haemodialysis

Serum creatinine concentration (mg/dl)							
				Pre-haemodialysis	**Post-haemodialysis**		
Age group (in years)	No. of patients	Gender		Mean ± SD	Mean ± SD	T-value	P-value
		M	F				
25-34	10	6	4	8.823 ± 2.520	3.044 ± 1.083	6.321	0.0001
35-44	24	11	13	10.92 ± 3.577	4.263 ± 1.806	8.412	0.0001
45-54	17	10	7	11.35 ± 2.708	4.419 ± 1.445	9.314	0.0001
55-64	12	8	4	9.096 ± 2.172	3.661 ± .1.299	7.440	0.0001
65+	16	9	7	10.03 ± 2.109	4.334 ± 1.978	7.875	0.0001
(Data are presented as Mean ± SD- Standard Deviation; n- Number of subjects; M-Male; F- Female; T-value; Student test value; P ≤ 0.05 significant-Statistical significance)							

The efficiency of haemodialysis was evaluated in 79 patients in separate age groups with ESKD using urea-reduction- ratio (URR) (Table 6 and Figure 1). The findings indicate that 4 (5.1%) patients had URR equal or less than 10% and of those, 2 (2.5%) patients were aged between 25 and 34 years,1(1.3%) patient was aged between 55 and 64 years, while another 1 (1.3%) patient was aged 65 and above (Table 6 and Figure 1). The data demonstrated that 14 (17.7%) patients had URR between 11-20%, and 2 (2.5%) of those patients are aged between 25 and 34 years, 4 (5.1%) patient were aged between 35 and 44 years, 5 (6.3%) patients were aged between 45 and 54 years, 1 (1.3%) patient was aged between 55 and 64 years and 6 (7.6%) patients were aged between 65 years and above. Also, 28 (35.4%) patients had URR between 21% and 30% and of those, 3 (3.8%) patients were aged between 18625 and 34 years and between 45 and 54 years, respectively, 11 (13.9%) patients were aged between 35 and 44 years, 5 (6.3%) patients were aged between 55 and 64 years while 6 (7.6%) patients were aged 65 years and above. The data also showed that 25 (31.6%) patients had URR between 31 - 40% and of those, 3 (3.8%) patients were aged between 25 and 34 years and 65 years and above, respectively, 7 (8.9%) patients were aged between 35 and 44 years, 8 (10.1%) patients were aged between 45 and 54 years, 4 (5.1%) patients were aged between 55 and 64 years. The data revealed that 6 (7.6%) patients had URR between 41 and 50%, of those, there was 1 (1.3%) patient with the age between 35 and 44 years, 45 and 54 years and 55 and 64 years, with remain 3 (3.8%) patients were aged 65 years and above. Of note, 1 (1.3%) patient aged between 35 and 44 years and 65 years and above had URR between 51- 60% and above 65%, respectively (Table 6 and Figure 1).

Table 6. Distribution of urea-reduction-ration (URR) in 79 patients on haemodialysis

Age group (in years)	25-34	35-44	45-54	55-64	65+	Total %
URR (%) (n =79)						
≤ 10	2(2.5%)	0	0	1(1.3%)	1(1.3%)	4 (5.1%)
11-20	2(2.5%)	4 (5.1%)	5(6.3%)	1(1.3%)	2(2.5%)	14(17.7%)
21-30	3(3.8%)	11(13.9%)	3(3.8%)	5(6.3%)	6(7.6%)	28(35.4%)
31-40	3(3.8%)	7(8.9%)	8(10.1%)	4 (5.1%)	3(3.8%)	25(31.6%)
41-50	0	1(1.3%)	1(1.3%)	1(1.3%)	3(3.8%)	6(7.6%)
51-60	0	1(1.3%)	0	0	0	1(1.3%)
65≤	0	0	0	0	1(1.3%)	1(1.3%)
Total	10(12.7%)	24(30.4%)	17(21.5%)	12(15.2%)	16(20.3%)	79(100%)

URR-Urea reduction ratio; n - Number of subjects; ≤ - Greater than or equal to; % - Percentage

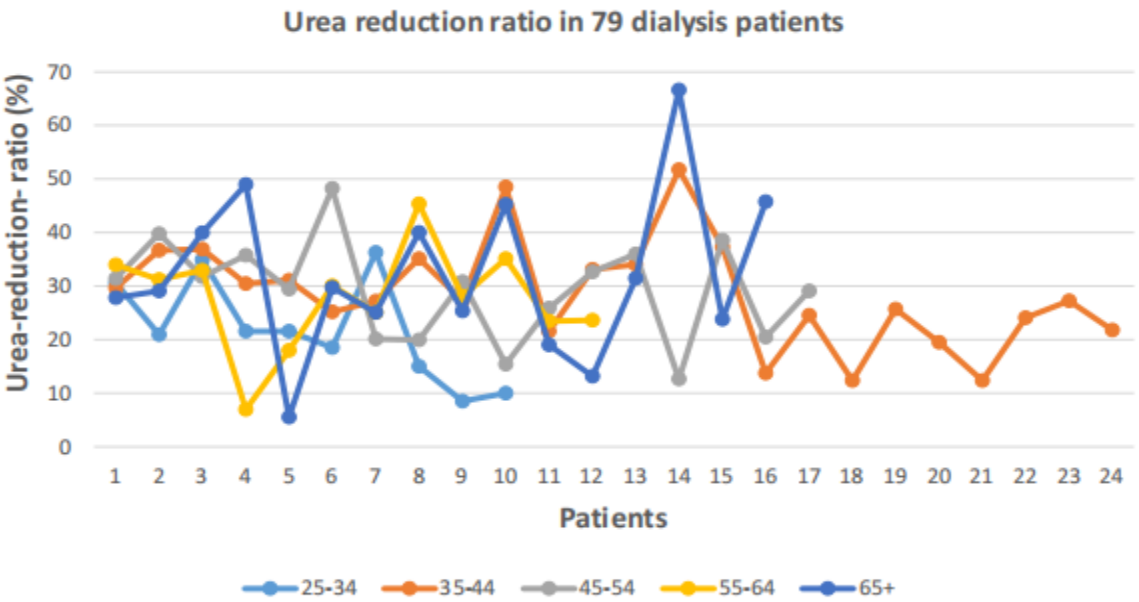

Figure 1. Distribution of urea-reduction-ration in 79 patients on haemodialysis

Discussion

The findings of the study demonstrate that in Lesotho, more males were enrolled in haemodialysis compared to female since the opening of renal unit centre. This is in line with an international prospective cohort study conducted in 12 countries which demonstrates that in all age groups, 59% of the males were on haemodialysis compared to 41% of the female (Hecking M et al.,2014). Although, the exact reasons for this behaviour may be uncertain, this may be attributed to lifestyle behaviours such as smoking, alcohol abuse, untreated or late diagnosis of comorbidities (including HTN, DM and HIV) in males than females which are high risk factors for ESKD. Indeed, (Simons et al., 2023) reported that male patients have lower service engagement than females of the same age (Simons et al., 2023). The findings in the present study showed that patients aged between 45 years and above diagnosed with HIV, HTN, DM or combination of all three comorbidities (HTN, HIV, DM), CCF urinary obstruction, various infections such as UTIs are prone to kidney damage leading to ESKD. Similarly, (Mallappallil et al., 2014) and (Damtie et al., 2018) revealed that there is a high burden of ESKD in patients aged between 45 and 64 years due to a rising prevalence of comorbidities and risk factors such as HTN, DM and HIV predisposing patients to ESKD or in older age above 65 years due to a reduction of estimated glomerular filtration rate (e-GFR) which decreases proportionally with aging. Additionally, HIV is the leading comorbidity at young age group (25 to 34 years) and middle age group (35 to 54 years) while HTN and DM are the leading comorbidities in older age (55 years and above) in Motebang government hospital. (Ando M & Ando Y, 2019) and (Chitja et al., 2021) also revealed that HIV, HTN, and DM are the three global leading comorbidities predisposing patients to the burden of ESKD. Anaemia is a common complication of chronic kidney disease (CKD) caused by insufficiency of the erythropoietin (EPO) by the proximal tubules in the kidneys (Jalalzadeh M, 2021). All patients in this study with ESKD and undergoing haemodialysis had anaemia.

The findings of the study revealed that there was a high mortality in males than in females, with more deaths occurring with old age (55 years and above) and middle age (45 to 54 years). This may be associated with high prevalence of HIV, HTN and DM which are the leading comorbidities in haemolysis patients with ESKD enrolled in Motebang hospital. A cohort study in 2021 conducted in the same renal unit between 2017 and 2018 also revealed high prevalence of HIV, HTN and DM in 233 ESKD patients (Chitja Met al., 2021). In 2012 and 2017, the WHO and LEPHIA survey studies showed that the prevalence of HTN was 31%, DM (1.3%) while HIV was 25% in Lesotho10,11(World Health Organization (WHO), 2018; Lesotho Population-Based HIV Impact Assessment (LePHIA2016-2017), 2018). Therefore, it's not surprising that the population of Lesotho between 25 years and above 65 years had ESKD. Similarly, all the patients had anaemia due to ESKD. More haemolysis patients with ESKD enrolled in Motebang renal unit died between the year 2019 and 2020. Although the reasons may be uncertain, this may be associated with COVID-19 pandemic. A systematic review study showed that patients with ESKD maintained on haemodialysis were at risk of death during the COVID-19 pandemic[0].

Biochemical evaluations of biomarkers such as serum urea, BUN and creatinine to assess kidney function should be conducted in patients undergoing haemodialysis. The study

findings showed a significantly high levels of serum urea, BUN and creatinine before the dialysis compared to the post- dialysis levels of serum urea, BUN and creatinine. Likewise, (Nisha et al., 2017) reported high serum urea, BUN and creatinine before dialysis compared to the same levels after the dialysis. Serum urea, BUN and creatinine are the metabolic waste products produced in the body and excreted via the kidneys or through haemodialysis in patients with ESKD (Liang KV et al., 2019).

Evaluation of the haemodialysis efficiency in patients with ESKD is of paramount importance to ensure an adequate removal of the biochemical markers such as serum urea, BUN and creatinine at least thrice a week()13. Urea-reduction-ratio is the simplest predominant approach for measurement of minimum adequacy clearance of biochemical waste products in patients with ESKD via haemodialysis (Liang KV et al., 2019). The study findings indicated that at all age groups, the majority of the patients had URR between 21 and 30% while only one patient had URR above 65%. According to the KDOQI standards recommendations, URR > 65% indicate maximum haemodialysis adequacy (Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines, 2006). Therefore, the study findings showed that the majority of patient's haemodialysis adequacy was minimal. This can correlate with serum urea and creatinine levels after haemodialysis which were significantly higher than normal ranges indicating inadequate haemodialysis. Although it is expected that patients with ESKD receive adequate haemodialysis, similar trend was observed in a clinical study that showed URR mean of 41.83% (Chijioke A et al., 2009). Contrary to the study findings, a cross-sectional study from Indonesia showed that more patients at all age groups received adequate haemodialysis with URR mean of 70.74%(Sartika KD & Sunaka IW, 2022).

Implications of the study

Creatinine and urea commonly used in Motebang government hospital for monitoring of end-stage kidney disease dose not fully assess the haemodialysis adequacy. Absence of e-GFR calculation and Urea reduction ratio means monitoring is in adequate.

The future research will focus mainly on the application of the Modification of Diet in Renal Disease (MDRD) and Chronic Kidney Disease-Epidemiology Collaboration (CKD-Epi) equations for calculating estimated glomerular filtration rate in patients with ESKD in Motebang government hospital.

Conclusion

The major leading risk factors to the prognosis of end-stage kidney disease especially in older people in Lesotho include HIV, HTN and DM. All the end-stage kidney disease in Motebang government hospital had anaemia.

Limitations

This study has several limitations. The available records in the renal unit do not fully provide outline of prognosis of the patient from one chronic kidney disease stage to another until the patients were diagnosed with ESKD because e-GFR was only indicated from the results obtained from the private laboratory. Lastly, it was estimated that approximately 186 patients were enrolled from 2017 up to 2023, but 142 patient charts were reviewed because some data charts were missing.

Recommendations

Different strategies for screening, early diagnosis and good management of these comorbidities at primary healthcare level should be strengthened to limit progression to ESKD. Urea-reduction-ratio in patients with ESKD should be conducted routinely as the part of the blood monitoring of biomarkers such as serum haemoglobin, urea, and creatinine.

Abbreviations

BUN, blood-urea- nitrogen; CKD-Epi, Chronic Kidney Disease-Epidemiology Collaboration; DM, diabetes mellitus; e-GFR estimated glomerular filtration rate; ESKD, end- stage kidney disease; F, Female; GBD, global disease burden; g/dl-grams per deciliter; Hb-haemoglobin; HIV, human immune virus; HTN, hypertension; IQR, interquartile range; KDIGO, kidney disease improving global outcomes; KDOQI, kidney disease outcome Initiative; LePHIA, Lesotho population-based HIV impact assessment; M, male; MOH-REC, ministry of health research ethics committee; MDRD, Modification of Diet in Renal Disease; NUL-IRB, National University of Lesotho international review board; SD, standard deviation;URR, urea-reduction-ration; USA, United State of America; WHO, world health organisation.

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