Chapter

Urine Creatinine Excretion in HIV and Non-HIV Subjects

Ernest Ndukaife Anyaholu

Abstract

This study assessed urine creatinine in spot and 24-hour samples in HIV and non-HIV population. We categorized dilute urine as a 24-hour urine creatinine <300 mg, concentrated urine as a 24-hour urine creatinine >3000 mg, and normal urine as a 24-hour urine creatinine 300–3000 mg. Association of variables with creatinine was evaluated. In HIV subjects, the mean spot urine creatinine was 137.21 ± 98.47 mg/dl and a 24-hour urine creatinine was 1507 ± 781 mg. The prevalence of dilute urine was 0.5%, normal urine 93.1%, and concentrated urine 6.4%. 20-hour urine creatinine was associated with serum LDL, and HDL. Concentrated urine was correlated with a 24-hour urine osmolality (r = 0.95), serum HDL (r = −0.73), CD4 cells count (r = −0.71), and BMI (r = 0.74). Dyslipidemia was common in HIV subjects with concentrated urine. In non-HIV subjects, the mean spot urine creatinine was 148 ± 167 mg/dl and the 24-hour urine creatinine was 1203 ± 316 mg. The 24-hour urine creatinine was within the normal range. The spot urine creatinine significantly correlated with BMI, spot urine protein, spot urine osmolality, 24-hour urine protein, 24-hour urine creatinine, serum creatinine, serum cholesterol, and serum LDL. Conversely, the 24-hour urine creatinine significantly correlated with 24-hour urine volume, serum creatinine, and serum cholesterol. The spot urine protein and 24-hour urine protein were predictors of spot urine creatinine. Serum creatinine was a predictor of 24-hour urine creatinine. Proteinuric renal abnormalities were common.

Keywords: HIV, urine creatinine, spot urine creatinine, 24-hour urine creatinine, CD4 cell count, concentrated urine, dilute urine, abnormal weight, dyslipidemia, proteinuria

1. Introduction

1.1 Impact of HIV

Human immunodeficiency virus infection is a world healthcare burden with sub-Saharan Africa as a geographic area accounting for about 70% of HIV-infected persons [1]. In Nigeria the prevalence of HIV is 3.7% [1]. HIV infection directly or indirectly affects most organs of the body [2]. In like manner, tons of physiological responses are also altered by HIV disease process [3–5].

1.2 Factors which may influence creatinine

Creatinine is produced by the muscles, degraded within the liver, and efficiently excreted by the kidney at a rate that is not only constant but is additionally modulated by weight, gender, and age [6].

Many environmental, physiologic, and disease conditions may impact on daily urine creatinine excretion. Excretion of creatinine is further altered by exogenous substances such as cocaine and heavy metals which include arsenic and cadmium seen within the bioenvironment related to environmental pollution. Others include meat consumption and medications such as cimetidine and trimethoprim. Consequently, urine creatinine is employed in monitoring bioenvironmental pollutants and substance use [7–9].

1.3 Variability of daily urine creatinine

There is high variability of the values of daily urine creatinine excretion in normal healthy state [10]. Impaired renal function usually results in poor renal secretion of creatinine in urine; urine creatinine decreases as renal function impairment increases [11].

1.4 Identified factors of high and low 24-hour urine creatinine

Studies have identified some associated factors of high 24-hour urine creatinine or concentrated urine. They include age, sex, race, body mass index, hypertension, water intake, and blood osmolality [12]. At the other pole, low 24-hour urine creatinine or dilute urine was reported to be associated with glomerular filtration rate, an older age, diabetes, and lower levels of body mass index, proteinuria, and protein intake [11]. Another important use of urine creatinine is for evaluating the completeness of 24-hour urine sample collection [13].

1.5 A necessity for routine assessment of urine creatinine in HIV and non-HIV subjects

Studies are sparse on urine creatinine in HIV and non-HIV subjects originating from Nigeria. We have, therefore, launched to evaluate urine creatinine and factors which influence low and high urine creatinine in these groups of subjects.

2. Methods

2.1 Study location and population

This was a cross-sectional study, comprising 375 HIV-positive subjects and 136 subjects recruited from an HIV clinic and also the general outpatient clinic, respectively, of the Federal Medical Centre, Owerri, Nigeria. The study was disbursed and carried out between April and August 2011. The standards for inclusion were HIV-positive status for the HIV subjects and HIV-negative status for the non-HIV participants. For both groups of subjects, another criterion was age range of 16–65 years. The themes excluded from the study were people who had adrenal, pituitary, and renal diseases, terminal illness, and pregnancy. For the non-HIV subjects, the inclusion criteria were similar, but those with HIV-positive status were excluded.

2.2 Ethics approval

The study was approved by the ethics research committee of the hospital. Its approval reference number was FMC/HCS/VOL II and was dated 16 March, 2011. Informed written consent was obtained from all the themes participated within the study.

2.3 Variables, data collection, and sample analyses

With the help of a questionnaire, demographic, anthropometric, and other relevant data were obtained from the themes. The purpose of the study was explained to the themes. The age, gender, place of origin, and domicile were obtained. Height was measured and recorded in meter (m). Weight was measured employing a weighing scale. Body mass index was taken as the ratio of weight/height^2 (kg/m^2).

The study participants were clearly instructed on the way to collect 24-hour urine sample. At the conclusion of the 24-hour urine sample collection, blood samples, and daytime random spot urine samples were collected. Spot urine creatinine, spot urine osmolality, and spot urine protein from the random spot urine samples were performed. Also from the 24-hour urine samples collected, 24-hour urine protein, 24-hour urine creatinine, and 24-hour urine osmolality were performed. Serum creatinine was performed on the blood samples collected. Freezing point depression assay was used to determine osmolality, protein by photometric method, and creatinine by modified Jaffe's method. Creatinine clearance and spot urine creatinine/osmolality ratio were calculated. HIV screening and confirmatory tests, fasting serum lipid profile, CD4 cell count, and hemoglobin were performed.

2.4 Potential risk variables analyzed

The potential associated factors of dilute and concentrated urine evaluated were CD4 cells, spot urine protein, spot urine osmolality, 24-hour urine osmolality, 24-hour urine protein, spot urine creatinine/osmolality ratio, creatinine clearance, serum cholesterol, serum low-density lipoprotein cholesterol, serum triglyceride, and serum high-density lipoprotein cholesterol.

2.5 Statistical analyses

The data were analyzed using SPSS version 17.0 (SPSS Inc. Chicago, IL, USA). The distribution and characterization of clinical and laboratory variables within the study participants with different levels of 24-hour urine creatinine were analyzed using cross-tabulation, whereas statistical significance of association of these variables with 24-hour urine creatinine levels was evaluated using Student's t-test. Correlation statistics were used to determine the association of those variables with concentrated urine on the one hand and with dilute urine on the other hand. The strength of variables to predict dilute urine and concentrated urine was determined using multivariate linear regression analyses. $P < 0.05$ was taken as statistically significant.

2.6 Definition of terms

Normal urine creatinine: 24-hour urine creatinine 300–3000 mg. Low urine creatinine or dilute urine: 24-hour urine creatinine <300 mg. High urine creatinine or concentrated urine: 24-hour urine creatinine >3000 mg.

3. Results

3.1 Results in HIV patients

3.1.1 Age, spot urine, and 24-hour urine creatinine in HIV patients

Out of the 393 participants studied, 18 were excluded due to errors from incomplete sample collection. Their mean age was 39 ± 11 years. For all the HIV participants, the mean spot urine creatinine was 137.21 ± 98.47 (mg/dl), minimum value 13.3 mg/dl, maximum value 533.3 mg/dl, and range 520.0 mg/dl. The mean 24-hour urine creatinine was 1507 ± 781 mg, minimum value 206 mg, maximum value 4849 mg, with a range of 4643 mg (**Table 1**).

3.1.2 Prevalence of dilute and concentrated urine and factors of 24-hour urine

Two (0.5%) of the HIV subjects have 24-hour urine creatinine <300 mg, 349 (93.1%) have 300–3000 mg, and 24 (6.4%) have >3000 mg. Serum low-density lipoprotein cholesterol was significantly associated with 24-hour ($p = 0.001$) in these HIV subjects. Two subjects have 24-hour urine creatinine <300 mg, and both of them have borderline serum low-density lipoprotein cholesterol. Twenty-four subjects have high urine creatinine, and all of them have desirable serum low-density lipoprotein cholesterol (**Table 2**).

3.1.3 Dilute urine, concentrated urine, and serum HDL in HIV patients

There was a significant association between serum high-density lipoprotein cholesterol and 24-hour urine creatinine, $p = 0.028$, in the HIV subjects. Two subjects

Variables (mean ± SD)	HIV subjects
Body mass index (kg/m^2)	26.2 ± 5.4
Hemoglobin (g/dl)	11.2 ± 1.8
CD4 cells/ml (median)	391
SUOsm (mOsm/kgH_2O)	464 ± 271
Spot urine protein (mg/dl)	11.89 ± 19.13
Spot urine creatinine (mg/dl)	137.21 ± 98.47
24-hour urine protein (g)	0.187 ± 0.290
24-hour urine creatinine (mg)	1507 ± 781
24HUOsm (mOsm/kgH_2O)	564 ± 501
SUCOR (mg/dl/mOsm/kgH_2O)	0.422 ± 0.486
Cholesterol (mmol/l)	4.26 ± 0.90
Triglyceride (mmol/l)	1.23 ± 0.37
HDL (mmol/l)	1.18 ± 0.39
LDL (mmol/l)	2.05 ± 0.58
Creatinine clearance (mls/min)	91.42 ± 22.98

SD, standard deviation; SUOsm, spot urine osmolality; 24HUOsm, 24-hour urine osmolality; SUCOR, spot urine creatinine/osmolality ratio; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol.

Table 1.
Variables in HIV patients.

Variables	24-hour urine creatinine levels (no (%))			Chi-square	Likelihood ratio	P value
	<300 mg	300–750 mg	>750 mg			
BMI (kg/m^2) < 18.5	0 (0.0%)	22 (91.7%)	2 (8.3%)	8.702	0.143	0.191
18.5–24.9	0 (0.0%)	124 (96.9%)	4 (3.1%)			
25.0–29.9	2 (1.4%)	128 (88.9%)	14 (9.7%)			
≥30	0 (0.0%)	75 (94.9%)	4 (5.1%)			
CD4 cell count <200	0 (0.0%)	41 (97.1%)	4 (8.9%)	0.781	0.614	0.677
≥200	2 (0.6%)	307 (93.3%)	20 (6.1%)			
Hb (g/dl) ≥12.0	2 (1.6%)	108 (88.5%)	12 (9.8%)	9.644	0.107	0.140
10.0–11.9	0 (0.0%)	163 (96.4%)	6 (3.6%)			
7.0–9.9	0 (0.0%)	72 (92.3%)	6 (7.7%)			
<7.0	0 (0.0%)	6 (100.0%)	0 (0.0%)			
ClCr (mls/min) ≥ 90 mls/min	0 (0.0%)	183 (92.0%)	16 (8.0%)	5.229	0.204	0.265
60–89	2 (1.4%)	135 (94.4%)	6 (4.2%)			
30–59	0 (0.0%)	31 (93.9%)	2 (6.1%)			
24 HUP <0.300 g	2 (0.6%)	301 (93.8%)	18 (5.6%)	8.018	0.178	0.237
≥0.300 g	0 (0.0%)	48 (88.9%)	6 (11.1%)			
FSLP (mmol/l)						
CholT Des (<5.2)	2 (0.6%)	308 (92.5%)	23 (6.9%)	1.618	0.806	0.659
BorderL (5.2–6.2)	0 (0.0%)	35 (97.2%)	1 (2.8%)			
High (>6.2)	0 (0.0%)	6 (100.0%)	0 (0.0%)			
LDL Des (<2.6)	0 (0.0%)	284 (92.2%)	24 (7.8%)	14.609	<0.001	0.001
BorderL (2.6–4.1)	2 (3.0%)	64 (97.0%)	0 (0.0%)			
HDL Low (<1)	2 (1.5%)	124 (95.4%)	4 (3.1%)	7.317	0.016	0.028
High (≥1)	0 (0.0%)	225 (91.8%)	20 (8.2%)			
TG Des (<1.7)	2 (0.6%)	311 (92.3%)	24 (7.1%)	3.150	0.449	0.790
BorderL (1.7–2.2)	0 (0.0%)	29 (100.0%)	0 (0.0%)			

Variables	24-hour urine creatinine levels (no (%))			Chi-square	Likelihood ratio	P value
	<300 mg	300–750 mg	>750 mg			
High (>2.2)	0 (0.0%)	8 (100.0%)	0 (0.0%)			

LHR, likelihood ratio; BMI, body mass index; Hb, hemoglobin; ClCr, creatinine clearance; 24HUP, 24-hour urine protein; FSLP, fasting serum lipid profile; CholT, total cholesterol; Des, desirable; BorderL, borderline; LDL, low-density lipoprotein cholesterol; HDL, high-density lipoprotein cholesterol; TG, triglyceride.

Table 2.
Distribution and characterization of variables at different levels of 24-hour urine creatinine in HIV-positive patients (n = 375).

have 24-hour urine creatinine <300 mg, and both have desirable serum high-density lipoprotein cholesterol <1 mg/dl. Twenty-four subjects have 24-hour urine creatinine >3000 mg. Out of this number, 83.3% have high serum high-density lipoprotein cholesterol, whereas 16.7% have desirable serum high-density lipoprotein cholesterol. This showed that the prevalence of high urine creatinine increased as serum high-density lipoprotein cholesterol increased (**Table 2**).

3.1.4 Dissociation and association between daily urine creatinine excretion and variables in HIV patients

There was no significant association between 24-hour urine creatinine and body mass index, p = 0.191; serum total cholesterol, p = 0.659; creatinine clearance, p = 0.265; 24-hour urine protein, p = 0.237; CD4 cell count, p = 0.677; serum triglyceride, p = 0.790; and hemoglobin, p = 0.140 in the HIV subjects (**Table 2**). Significant correlation was obtained between 24-hour urine creatinine and spot urine creatinine (p = 0.19), 24-hour urine volume (p = 0.004), spot urine creatinine/osmolality ratio (<0.001), serum low-density lipoprotein cholesterol (p = 0.31), creatinine clearance (p < 0.001), and serum creatinine (<0.001) in the treatment-naïve HIV subjects. Hemoglobin, spot urine protein, spot urine osmolality, 24-hour urine protein, 24-hour urine osmolality, serum cholesterol, serum high-density lipoprotein cholesterol, and serum triglyceride did not have significant correlation with 24-hour urine creatinine (**Table 3**).

3.1.5 Correlates of daily urine creatinine excretion in HIV patients

There was a very strong correlation between 24-hour urine creatinine >3000 mg and 24-hour urine osmolality (r = 0.95), body mass index, (r = 0.74), CD4 cell count, (r = −0.71), and serum high-density lipoprotein cholesterol (r = −0.73) in the HIV subjects. However, there was a moderate correlation between 24-hour urine creatinine and 24-hour urine volume (r = 0.58) and hemoglobin (r = −0.43). Conversely, there was a poor correlation between spot urine creatinine and body mass index (r = 0.131, p = 0.009)), spot urine protein (r = 0.183, p = <0.001), spot urine osmolality (r = 0.288, p = <0.001), 24-hour urine volume (r = −0.111, p = 0.032), and creatinine clearance (r = 0.108, p = 0.036) (**Table 4**).

3.1.6 Predictors of concentrated urine in HIV patients

Multivariate linear regression of 24-hour urine creatinine >3000 mg with its potential risk factors was voided as the colinearity variance was skewed due to the small subpopulation (24) that have 24-hour urine creatinine >3000 mg.

Variables	Correlation coefficient (r)	P value
Body mass index	−0.036	0.470
Hemoglobin (g/dl)	0.075	0.117
Spot urine protein	0.044	0.538
Spot urine creatinine	0.129	0.019
Spot urine osmolality	0.107	0.058
24-hour urine protein	0.035	0.625
24-hour urine osmolality	0.063	0.167
24-hour urine volume	0.143	0.004
SUCOR	0.288	<0.001
Serum creatinine	0.290	<0.001
Serum cholesterol (total)	0.074	0.242
Serum Triglyceride	−0.075	0.189
Serum HDL	0.029	0.542
Serum LDL	−0.109	0.031
Creatinine clearance	0.367	<0.001

SUCOR, spot urine creatinine osmolality ratio; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol.

Table 3.
Correlation of 24HUCr with variables in HIV patients (n = 375).

Variables	Correlation coefficient (r)	P value
Body mass index	0.744	<0.001
Hb (g/dl)	−0.427	<0.001
Spot urine protein	0.397	<0.001
Spot urine creatinine	0.371	<0.001
Spot urine osmolality	−0.549	<0.001
24-hour urine protein	−0.109	0.001
24-hour urine osmolality	0.952	<0.001
24-hour urine volume	0.578	<0.001
Serum creatinine	−0.198	<0.001
Serum cholesterol (total)	0.215	<0.001
Serum triglyceride	0.001	0.925
Serum HDL	−0.729	<0.001
Serum LDL	0.289	<0.001
Hemoglobin	−0.427	<0.001

SUCOR, spot urine creatinine osmolality ratio; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol.

Table 4.
Correlation of 24HUCr > 3000 mg with variables in HIV patients (n = 24).

3.2 Results in non-HIV subjects

3.2.1 Values of spot urine and 24-hour urine creatinine in non-HIV subjects

Out of the 136 non-HIV subjects enrolled in this study, females constituted 72.1% and males 27.9%. Their mean age was 39 ± 12 years. They all have complete data or sample collection, and there was no attrition. The value of the mean spot urine creatinine was 148 ± 167, minimum value 14.7 mg/dl, and maximum value 746.7 mg/dl with a range of 732.0 mg/dl. Further, the value of the mean 24-hour urine creatinine was 1203 ± 316, minimum value 651.0 mg, maximum value 2320 mg, and range 1669.0 mg. The mean values of all other variables are depicted in **Table** 5.

For all the subjects the mean 23-hour urine creatinine was in the normal range (300–3000 mg). The potential risk factors for concentrated or dilute urine were voided and could not be distributed or characterized.

3.2.2 Correlates of spot urine creatinine

There was a significant correlation between spot urine creatinine and body mass index ($r = 0.225$, $p = 0.009$), spot urine protein ($r = 0.292$, $p = 0.001$), spot urine osmolality ($r = 0.223$, $p = 0.009$), serum low-density lipoprotein cholesterol ($r = 0.282$, $p = 0.001$), 24-hour urine protein ($r = -0.187$, $p = 0.030$), 24-hour urine creatinine ($r = -0.178$, $p = 0.038$), serum creatinine ($r = -0.212$, $p = 0.013$), as well as serum cholesterol ($r = 0.246$, $p = 0.004$). In contrast, spot urine creatinine has no significant correlation with hemoglobin, 24-hour urine volume, 24-hour urine

Variables (mean ± SD)	**Subjects**
Body mass index (kg/m^2)	25.5 ± 6.5
Hemoglobin (g/dl)	12.9 ± 1.6
Serum creatinine (mg/dl)	0.88 ± 0.19
SUOsm ($mOsm/kgH_2O$)	334 ± 204
Spot urine protein (mg/dl)	7 ± 18
Spot urine creatinine (mg/dl)	148 ± 167
24-hour urine volume (ml)	1874 ± 681
24-hour urine protein (g)	0.095 ± 0.087
24-hour urine creatinine (mg)	1203 ± 316
24HUOsm ($mOsm/kgH_2O$)	160 ± 133
Cholesterol (mmol/l)	3.8 ± 1.2
Triglyceride (mmol/l)	1.2 ± 0.4
HDL (mmol/l)	1.2 ± 0.3
LDL (mmol/l)	2.3 ± 1.0
Creatinine clearance (mls/min)	93.0 ± 41.2

SD, standard deviation; SUOsm, spot urine osmolality; 24UOsm, 24-hour urine osmolality; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol.

Table 5.
Variables in non-HIV subjects (n = 136).

Variables	Correlation coefficient(r)	P value
Body mass index	0.225	0.009
Hemoglobin	0.024	0.782
Spot urine protein	0.292	0.001
Spot urine osmolality	0.223	0.009
24-hour urine protein	−0.187	0.030
24-hour urine creatinine	−0.178	0.038
24-hour urine volume	−0.097	0.259
24HUOsm	−0.165	0.055
Serum creatinine	−0.212	0.013
Serum cholesterol (total)	0.246	0.004
Serum Triglyceride	0.157	0.067
Serum HDL	0.137	0.112
Serum LDL	0.282	0.001
Creatinine clearance	0.024	0.782

HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; 24HUOsm, 24-hour urine osmolality.

Table 6.
Correlation of spot urine creatinine with variables in non-HIV subjects (n = 136).

osmolality, serum triglyceride, serum high-density lipoprotein cholesterol, as well as creatinine clearance (**Table 6**).

3.2.3 Correlates of 24-hour urine creatinine

Twenty-four-hour urine creatinine significantly correlated with 24-hour urine volume ($r = 0.213$, $p = 0.013$), serum creatinine ($r = 0.741$, $p < 0.001$), and spot urine creatinine ($r = -0.178$, $p < 0.001$). On the contrary, 24-hour urine creatinine did not significantly correlate with body mass index, hemoglobin, spot urine protein, spot urine osmolality, 24-hour urine protein, 24-hour urine osmolality, serum cholesterol, serum triglyceride, serum high-density lipoprotein cholesterol, as well as serum low-density lipoprotein cholesterol (**Table 7**).

Twenty-four-hour urine protein significantly correlated with 24-hour urine volume ($r = 0.213$, $p = 0.013$), serum creatinine ($r = 0.741$, $p < 0.001$), and spot urine creatinine ($r = -0.178$, $p < 0.001$).

3.2.4 Predictors of spot urine creatinine

The variables that predicted spot urine creatinine were spot urine protein ($p < 0.001$) and 24-hour urine protein ($p = 0.021$), whereas body mass index, serum creatinine, spot urine osmolality, 24-hour urine creatinine, serum cholesterol, and serum low-density lipoprotein cholesterol did not (**Table 8**).

3.2.5 Predictor of 24-hour urine creatinine in non-HIV subjects

Only one variable predicted 24-hour urine creatinine—serum creatinine ($p < 0.001$)—whereas spot urine creatinine and 24-hour urine volume did not (**Table 9**).

Body mass index	0.056	0.520
Hemoglobin	0.046	0.593
Spot urine protein	−0.083	0.337
Spot urine osmolality	−0.091	0.294
Spot urine creatinine	−0.178	0.038
24-hour urine protein	−0.027	0.753
24-hour urine volume	0.213	0.013
24-hour urine osmolality	0.106	0.220
Serum creatinine	0.741	<0.001
Serum cholesterol (total)	−0.032	0.708
Serum triglyceride	−0.008	0.925
Serum HDL	0.038	0.657
Serum LDL	−0.092	0.286
Creatinine clearance	0.634	<0.001

HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol.

Table 7.
Correlation of 24-hour urine creatinine with variables in non-HIV subjects.

Variables	Beta	T	P value	95% CI
Body mass index	0.107	1.160	0.248	−1.964–7.523
Serum creatinine	−0.200	−1.729	0.086	−282.537–23.785
Spot urine protein	0.312	3.760	<0.001	1.350–4.346
Spot urine osmolality	0.100	1.318	0.190	−0.045–0.225
24-hour urine protein	−0.184	−2.331	0.021	−53.513 0–0.354
24-hour urine creatinine	0.026	0.228	0.820	−105.945–133.584
Serum cholesterol	−0.136	−0.632	0.528	−1.952–1.007
Serum LDL	0.375	1.804	0.074	−0.148–3.199

CI, confidence interval; LDL, low-density lipoprotein cholesterol.

Table 8.
Multivariate linear regression of variables with spot urine creatinine in non-HIV subjects (n = 136).

Variables	Beta	T	P value	95% CI
Serum creatinine	0.723	26,353	<0.001	−1.065–0.814
Spot urine creatinine	−0.003	−0.097	0.923	0.000–0.000
24-hour urine volume	−0.038	−1.389	0.167	0.011–0.013

CI, confidence interval.

Table 9.
Multivariate linear regression of variables with 24-hour urine creatinine in non-HIV subjects (n = 136).

4. Discussion

4.1 Discussion in HIV patients

4.1.1 Prevalence of dilute urine in HIV patients

This study noted the prevalence of dilute urine or low urine creatinine of 0.5% and concentrated urine or high urine creatinine of 6.4% in HIV patients. It showed an association between high urine creatinine and serum low-density lipoprotein cholesterol, $p = 0.001$, as well as serum high-density lipoprotein cholesterol, $p = 0.028$. It further showed that high urine creatinine very strongly correlated with 24-hour urine osmolality ($r = 0.95$), body mass index ($r = 0.74$), CD4 cell count ($r = -0.71$), and serum high-density lipoprotein cholesterol ($r = -0.73$). In this study the prevalence of low urine creatinine was 0.5%. This is in disagreement with 8.1% documented by Barr et al. [14]. In the same vein, the observed 6.4% prevalence of high urine creatinine in this study was a bit higher than the 3.1% reported by Barr et al. [14] in the same study previously mentioned. Differences in study design perhaps might explain the observed difference in the prevalence. Whereas the subjects in this group of our study participants were HIV patients in Nigeria, their study participants were non-HIV from a US general population. In Romania, studies reported high chronic kidney disease prevalence in HIV patients who were on variable antiretroviral therapy duration [15–17]. These Romanian studies evaluated kidney disease using MDRD equation, a formula that incorporated serum creatinine in its utility. Glaringly, however, their study failed to analyze daily urine creatinine excretion.

4.1.2 Concentrated urine associated with serum LDL and HDL in HIV patients

This study demonstrated a significant association between high urine creatinine and serum low-density lipoprotein cholesterol as well as serum high-density lipoprotein cholesterol. Literature was sparse on the impact of high urine creatinine excretion on serum low-density lipoprotein cholesterol or serum high-density lipoprotein cholesterol. Nonetheless, in chronic kidney disease, low serum low-density lipoprotein cholesterol and low serum high-density lipoprotein cholesterol are characteristic components of dyslipidemia. Lipid synthesis by the liver is thought to be induced by proteinuria in kidney disease. Triglyceride-rich apolipoprotein B (apoB) containing complex lipoproteins, mark these syntheses. They have profound atherogenic potential which inadvertently will impact negatively on the kidney and subsequently affect urine creatinine excretion [18–20].

4.1.3 Concentrated urine associated with 24-hour urine osmolality in HIV patients

This study showed that there was very strong correlation between high urine creatinine and 24-hour urine osmolality ($r = 0.95$). A similar observation was reported in a study that assessed the utility of urine creatinine and urine osmolality in determining dilute or concentrated urine and therefore the factors that influenced these. That study observed that the quantum of associations depicted as a fraction in change was profoundly stronger with urine creatinine than urine osmolality. The report noted that urine osmolality, compared to urine creatinine, was influenced by daily total protein intake but failed to vary by diabetes status. Although this association seemed relevant, the study inferred that the plausibility of accepting the utilization of urine osmolality adjustment and water intake

prescription to enhance on the accuracy of spot urine samples provision for the monitoring of bioenvironmental pollution would in itself espouse the merit for further evaluations [12].

4.1.4 Concentrated urine associated with BMI in HIV patients

High urine creatinine has a high correlation with body mass index, r = 0.74, in this study. This is in conformity with the findings reported by Forbes et al. [21] with r = 0.99 and Baxmann et al. [22] with r = 0.74. These two studies differed in design as they were administered in a very general population, compared to the present index subpopulation of our study that was an HIV patient population. The marginally higher correlation seen within the Forbes et al. [21] study showed a rather higher correlation which could be adduced to urine creatinine evaluation in lean body mass, in subjects very likely to be underweight.

4.1.5 Inverse correlation between concentrated urine and CD4 cell count and HDL in HIV patients

In this study high urine creatinine has a high inverse correlation, r = −0.71, with CD4 cell count. A study has documented an association between low CD4 cells count and underweight in HIV subjects [23]. Perhaps, this might account for the high, albeit inverse, correlation between high urine creatinine and CD4 cell count noted in our study. We also observed in our study that high urine creatinine has a high but inverse correlation, r = −0.73, with serum high-density lipoprotein cholesterol. There was dearth of studies that assessed the link between serum high-density lipoprotein cholesterol and high urine creatinine.

4.1.6 Correlation between concentrated urine and 24-hour urine volume and anemia in HIV patients

This study showed that there was moderate correlation statistics between high urine creatinine and 24-hour urine volume (r = 0.58) and hemoglobin (r = −0.43). The higher the concentration of urine, the lower the hemoglobin, implying that anemia was associated with concentrated urine. Literature search did not reveal any study that evaluated the effects of urine volume or hemoglobin on urine creatinine.

4.2 Discussion in non-HIV patients

4.2.1 Absent abnormal urine concentration in non-HIV subjects

This study showed that low and high urine creatinine was absent within the outpatient population as all of them have 24-hour urine protein within the normal range.

4.2.2 Correlates of spot urine and daily urine creatinine excretion in non-HIV subjects

Spot urine creatinine correlated significantly with body mass index (r = 0.225, p = 0.009), spot urine protein (r = 0.292, p = 0.001), spot urine osmolality (r = 0.223, p = 0.009), 24-hour urine protein (r = −0.187, p = 0.030), 24-hour urine creatinine (r = −0.178, p = 0.038), serum creatinine (r = −0.212,

p = 0.013), serum cholesterol (r = 0.246, p = 0.004), and serum low-density lipoprotein cholesterol (r = 0.282, p = 0.001). Factors that significantly correlated with 24-hour urine creatinine were 24-hour urine volume (r = 0.213, p = 0.013), serum creatinine (r = 0.741, p < 0.001), and spot urine creatinine (r = −0.178, p < 0.001). Spot urine protein and 24-hour urine protein predicted spot urine creatinine, whereas only serum creatinine predicted 24-hour urine creatinine.

4.2.3 Only normal levels of urine creatinine in non-HIV subjects

In this study there was an absence of low and high urine creatinine in subjects attending the outpatient clinic. This disagrees with the prevalence of 8.1% of low urine creatinine and 3.1% of high urine creatinine reported by Barr et al. [14]. Their study was conducted in a US general population in contrast with ours that was done in a general outpatient clinic population in Nigeria. This difference in study design might have accounted for the observed differences between the two studies. Additionally, our study subjects were patients who might have presented to hospital for one illness or the other that might impact on urine creatinine.

4.2.4 Spot urine creatinine associated with BMI in non-HIV subjects

Our study showed that BMI was associated with spot urine creatinine but not with 24-hour urine creatinine. This observation is similar to that reported in two studies [14, 24]. Two studies further demonstrated that body mass index was a predictor of spot urine creatinine [24, 25], in contrast with our study which showed that body mass index did not predict spot urine creatinine and 24-hour urine creatinine. Urine creatinine, a function of body mass index, a measure of lean body mass, depends on muscle mass.

4.2.5 Spot urine and daily urine protein excretion were predictors of spot urine creatinine in non-HIV subjects

This study demonstrated that spot urine protein and 24-hour urine protein were predictors of spot urine creatinine. This was slightly similar to a study that found protein intake associated with urine creatinine [26]. We observed that these two variables were not associated with 24-hour urine creatinine. Protein in urine predicting spot urine creatinine, with 24-hour urine creatinine within the normal range, indicated that the subjects studied might have proteinuria even in the presence of normal renal filtration function.

Spot urine osmolality was associated with spot urine creatinine but did not predict it, in this study. The precise relationship between urine creatinine and urine osmolality has not been fully elucidated, even though the utility of the hypothetical ratios for estimation of daily urine protein excretion involving creatinine and osmolality has been established [27, 28].

4.2.6 Inverse correlation between spot urine creatinine and daily urine creatinine excretion in non-HIV subjects

There was an inverse correlation between spot urine creatinine and 24-hour urine creatinine observed in this study. This implied that as spot urine creatinine increased, 24-hour urine creatinine declined and vice versa. Studies were sparse on the link between spot urine creatinine and 24-hour urine creatinine.

4.2.7 Association between serum creatinine and spot urine creatinine in non-HIV subjects

The study showed that serum creatinine was associated with spot urine creatinine. Serum creatinine in normal state is maintained at a reasonably constant level as excess creatinine produced by the body or taken exogenously is excreted in urine. This produces variability in the amount of creatinine in urine excreted by an individual and between different individuals [29]. However, elevated serum creatinine would be observed in impaired renal function, associated with reduced urine creatinine [30]. Expectedly, serum creatinine was a predictor of 24-hour urine creatinine in this study.

4.2.8 Spot urine creatinine associated with HDL and LDL in non-HIV subjects

Serum cholesterol and serum low-density lipoprotein cholesterol were associated with spot urine creatinine, as observed in our study. Lipid abnormalities have been described in renal disease associated with reduced urine creatinine excretion [31, 32]. This might suggest that our study subjects might have renal impairment.

4.2.9 Daily urine creatinine excretion associated with daily urine volume in non-HIV subjects

We noted that 24-hour urine volume was associated with 24-hour urine creatinine in this study. A related study reported an association between 24-hour urine volume and creatinine clearance [33]. In contrast, our study did not find any association between 24-hour urine creatinine and creatinine clearance. Nonetheless, urine volume tends to decrease with decreasing creatinine clearance, and 24-hour urine creatinine is a function of creatinine clearance. This probably would explain the association between 24-hour urine volume and 24-hour urine creatinine observed in this study.

5. Conclusion

The prevalence of low urine creatinine and high urine creatinine was low. Twenty-four-hour urine osmolality, body mass index, CD4 cell count, and hemoglobin were strong correlates of high urine creatinine. Dyslipidemia was common in HIV subjects who have high urine creatinine. Low and high urine creatinine was absent in non-HIV subjects. Proteinuric renal abnormalities, abnormal weight, and dyslipidemia were common in these non-HIV subjects with normal urine creatinine. There is need for clinicians to routinely conduct urine creatinine and further search for dyslipidemia, abnormal weight, depressed immunity, and anemia in HIV subjects with dilute or concentrated urine in the early stages of the infection. There is also a necessity for clinicians to routinely conduct urine creatinine and further explore for abnormalities of lipids, renal function, and weight changes in subjects with normal urine creatinine in non-HIV subjects.

6. Limitations of the study in HIV subpopulation

A larger HIV study population would have been better, as it would have prevented skewing of the colinearity that rendered null and void the multivariate linear regression of urine creatinine with the variables. Staging of HIV infection for all the

subjects and concisely defining the time from the diagnosis of HIV infection in these subjects to the conduct of this study were not done but would have contributed in further defining the link between urine creatinine and these factors. Similarly, the non-HIV study population was small. A way larger sample size would have shown a proportion of these with low and high urine creatinine, however little they may be, and also the potential risk factors of dilute and concentrated urine in this population.

Competing interests

The author declares no competing interests.

Permission

The methodology and tables in this book chapter are excerpts from articles published by Anyabolu [34, 35].

Author details

Ernest Ndukaife Anyabolu
Renal Unit, Department of Internal Medicine, Chukwuemeka Odumegwu Ojukwu University, Awka, Nigeria

*Address all correspondence to: enhealer@yahoo.com

References

[1] UNAiDS. Global Report: UNAIDS Report on the Global AIDS Epidemic. 2013

[2] Chu C, Selwyn PA. Complications of HIV infection: A systems-based approach. American Family Physician. 2011;**83**(4):395-406

[3] Moir S, Fauci AS. B cells in HIV infection and disease. Nature Reviews. Immunology. 2009;**9**(4):235-245

[4] Segerstrom SC, Miller GE. Psychological stress and the human immune system: A meta-analytic study of 30 years of inquiry. Psychological Bulletin. 2004;**130**(4):601-630

[5] Shah K, Alio AP, Hall WJ, Luque AE. The physiological effects of obesity in HIV-infected patients. Journal of AIDS & Clinical Research. 2012;**3**:151

[6] Wyss M, Kaddurah-Daouk R. Creatine and creatinine metabolism. Physiological Reviews. 2000;**80**(3): 1107-1213

[7] Barr DB, Wang RY, Needham LL. Biologic monitoring of exposure to environmental chemicals throughout the life stages: Requirements and issues for consideration for the National Children's study. Environmental Health Perspectives. 2005;**13**(8):1083-1091

[8] Assessment of elevated creatinine. BMJ Best Practice. 2015;**141**(12):929-937

[9] Andreev E, Koopman M, Arisz L. A rise in plasma creatinine that is not a sign of renal failure: Which drugs can be responsible? Journal of Internal Medicine. 1999;**246**:247-252

[10] Waikar SS, Sabbisetti VS, Joseph V, Bonventre JV. Normalization of urinary biomarkers to creatinine during changes in glomerular filtration rate. Kidney International. 2010;**78**(5):486-494

[11] Tynkevich E, Flamant M, Haymann J-P, Metzger M, Thervet E, et al. Decrease in urinary creatinine excretion in early stage chronic kidney disease. PLoS One. 2014;**9**(11):e111949

[12] Yeh HC, Lin YS, Kuo CC, Weidemann D, Weaver V, et al. Urine osmolality in the US population: Implications for environmental biomonitoring. Environmental Research. 2015;**136**:482-490

[13] John AK, Cogswell ME, Campbell NR, Nowson CA, Legetic B. Accuracy and usefulness of select methods for assessing complete collection of 24-hour urine: A systematic review. Journal of Clinical Hypertension (Greenwich, Conn.). 2016;**18**(5):456-467

[14] Barr DB, Wilder LC, Caudill SP, Gonzalez AJ, Needham LL, et al. Urinary creatinine concentrations in the US population: Implications for urinary biologic monitoring measurements. Environmental Health Perspectives. 2005;**113**(2):192-200

[15] Horosanu GC, Streinu-Cercel A, Tudor AM, Streinu-Cercel A. A profile of specific risk factors for chronic kidney disease-mineral and bone disorder in Romanian HIV-positive patients. Journal of Contemporary Clinical Practice. 2016;**2**(1):18-24

[16] Streinu-Cercel A. Osteo-renal impairment in HIV infection. Germs. 2014;**4**(2):29

[17] Streinu-Cercel A, Sandulescu O, Ceapraga G, Manolache D, Stoica MA, Preotescu LL, et al. Prevalence of osteo-renal impairment in the Romanian HIV cohort. BMC Infectious Diseases. 2016;**16**(Suppl 1):93

[18] Vaziri ND. Molecular mechanisms of lipid disorders in nephrotic syndrome. Kidney International. 2003;**63**(5):1964-1976

[19] Trevisan R, Dodesini AR, Lepore G. Lipids and renal disease. Journal of the American Society of Nephrology. 2006;**17**(4 Suppl 2):S145-S147

[20] Muntner P, Coresh J, Smith C, Eckfeldt J, Klag MJ. Plasma lipids and risk of developing renal dysfunction: The atherosclerosis risk in communities study. Kidney International. 2000;**58**(1):293-301

[21] Forbes GB, Bruining GJ. Urinary creatinine excretion and lean body mass. American Journal of Clinical Nutrition. 1976;**29**(12):1359-1366

[22] Baxmann AC, Ahmed MS, Marques NC, Menon VB, Pereira AB, et al. Influence of muscle mass and physical activity on serum and urinary creatinine and serum cystatin C. Clinical Journal of the American Society of Nephrology. 2008;**3**(2):348-354

[23] Anyabolu EN. BMI and risk factors of underweight and obesity in HIV subjects in eastern Nigeria. World Journal of AIDS. 2016;**6**:8-15

[24] Bader M, Messerer P, Will W. Urinary creatinine concentrations in an industrial workforce and comparison with reference values of the general population. International Archives of Occupational and Environmental Health. 2013;**86**(6):673-680. DOI: 10.1007/s00420-012-0802-4

[25] Sinkeler SJ, Visser FW, Krikken JA, Stegeman CA, Homan van der Heide JJ, Navis G. Higher body mass index is associated with higher fractional creatinine excretion in healthy subjects. Nephrology Dialysis Transplantation. 2011;**26**(10): 3181-3188. DOI: 10.1093/ndt/gfq850 [Epub 3 Mar 2011]

[26] Neubert A, Remer T. The impact of dietary protein intake on urinary creatinine excretion in a healthy pediatric population. The Journal of Pediatrics. 1998;**133**(5):655-659

[27] Anyabolu EN, Chukwuonye II, Mabayoje M, Ejike A, Ijoma CK, et al. Comparison of spot urine protein/creatinine ratio, spot urine protein/osmolality ratio with measured 24-hour urine protein in HIV subjects in Nigeria. Journal of AIDS & Clinical Research. 2015;**6**:445. DOI: 10.4172/2155-6113.1000445

[28] Yang Y, Yian-Sheng X, Guang-Ming L, Zuo-Xiang L, Hua-bin S, et al. Establishment of equations for predicting 24-hour urine protein excretion and testing of their performance. Academic Journal Second Military Medical University. 2011;**31**:1113-1117

[29] Stiegel MA, Pleil JD, Sobus JR, Angrish MM, Morgan MK. Kidney injury biomarkers and urinary creatinine variability in nominally healthy adults. Biomarkers. 2015;**20**(6-7):436-452. DOI: 10.3109/1354750X.2015.1094136

[30] Winnett G, Cranfield L, Almond M. Apparent renal disease due to elevated creatinine levels associated with the use of boldenone. Nephrology Dialysis Transplantation. 2011;**26**(2):744-747. DOI: 10.1093/ndt/gfq663. [Epub 27 October 2010]

[31] Pandya V, Rao A, Chaudhary K. Lipid abnormalities in kidney disease and management strategies. World Journal of Nephrology. 2015;**4**(1):83-91

[32] Tsimihodimos V, Mitrogianni Z, Elisaf M. Dyslipidemia associated with chronic kidney disease. Open Cardiovascular Medicine Journal. 2011;**5**:41-48. DOI: 10.2174/1874192401105010041

[33] Schoen T, Blum J, Paccaud F, Burnier M, Bochud M, Conen D. Factors

associated with 24-hour urinary volume: The Swiss salt survey. BMC Nephrology. 2013;**14**:246. DOI: 10.1186/1471-2369-14-246

[34] Anyabolu EN. Urine creatinine in treatment-naïve HIV subjects in eastern Nigeria. The Pan African Medical Journal. 2016;**25**:139. DOI: 10.11604/pamj.2016.25.139.10580

[35] Anyabolu EN. Urine creatinine in a general out-patient population: Implications. Science Journal of Clinical Medicine. 2016;**5**(6):46-50. DOI: 10.11648/j.sjcm.20160506.11