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Urine Creatinine in a General Out-Patient Population: Implications

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Abstract: Some diseases, environmental pollutants and physiologic states may influence urine creatinine. Urine creatinine is not routinely evaluated in the general out-patient population. The objective of this study was to evaluate urine creatinine and factors that may influence it in subjects attending the general out-patient clinic in a tertiary hospital in Nigeria. This was a cross-sectional study involving subjects consecutively recruited from a general out-patient clinic in Federal Medical Centre, Owerri, Nigeria. Creatinine in spot and 24-hour urine samples and other relevant investigations were performed. Dilute urine or low urine creatinine was defined as 24-hour urine creatinine (24HUCr) <300mg, normal urine creatinine as 24HUCr 300 - 300mg, and concentrated urine or high urine creatinine as 24HUCr >3000mg.The association of variables with urine creatinine and the strength of variables to predict dilute and concentrated urine were determined. The mean spot urine creatinine (SUCr) of the subjects was 148±167mg/dl, minimum value 14.7mg/dl, maximum value 746.7mg/dl and range of values 732.0mg/dl. The mean 24HUCr was 1203±316mg, minimum value 651.0mg, maximum value 2320mg, and range of values 1669.0mg. All the subjects have 2HUCr in the normal range. Spot urine creatinine has significant correlation with body mass index, spot urine protein (SUP), spot urine osmolality, 24-hour urine protein (24HUP), 24HUCr, serum creatinine, serum cholesterol and serum low density lipoprotein cholesterol. In contrast, 24HUCr has significant correlation with 24-hour urine volume, serum creatinine and serum cholesterol. Spot urine protein and 24HUP predicted SUCr, while only serum creatinine predicted 24HUCr. Low and high urine creatinine were absent in subjects attending the general out-patient clinic. Proteinuric renal abnormalities were common in these subjects with normal urine creatinine. There is need for clinicians to routinely conduct urine creatinine and further search for renal damage, dyslipidemia and abnormal weight changes in the general out patients with normal urine creatinine.

Keywords: Urine Creatinine, Serum Creatinine, Proteinuria, General Out-Patient Clinic, Associated Factors, Nigeria

1. Introduction

In normal healthy state, the kidney excretes creatinine at a constant rate that varies with age, gender and weight. The production of creatinine takes place in the muscles while its degradation occurs in the liver. [1]

Urine creatinine excretion is influenced by many physiologic, environmental and disease conditions. The amount of creatinine excreted in urine is influenced by both endogenous production as well as by exogenous substances. These exogenous substances include some medications like trimethoprim and cimetidine, cocaine, heavy metals like cadmium and arsenic, and meat consumption. Consequently, substance use and monitoring of bioenvironmental pollutants are being achieved using urine creatinine. [2-4]

There is variability in the range of values of creatinine excreted in urine in a day, in normal healthy state. [5] The secretion of creatinine in urine decreases with impaired renal function, indicating that as renal impairment increases, urine creatinine decreases. [6]

Concentrated urine has been associated with race, body mass index (BMI), blood osmolality, hypertension, age, sex, and water intake. [7] At the other pole, older age, low BMI,

protein intake, glomerular filtration rate, proteinuria and diabetes were associated with dilute urine. [6]

The assessment of completeness of 24-hour urine sample collection is done using urine creatinine. [8]

There is a paucity of studies on urine creatinine in subjects attending the general out-patient clinics emanating from Sub-Saharan Africa. We have embarked on this study to evaluate urine creatinine in these subjects. This will help in identifying subjects with dilute and concentrated urine and the factors which influence urine creatinine with a view to instituting interventions that will stem down the attendant adverse outcomes in the general out patients.

2. Materials and Methods

This was designed a cross-sectional study in which 136 subjects were consecutively recruited from a general out-patient clinic of FMC, Owerri, Nigeria. It was conducted between April and August 2011. Those included in the study were 16-65 years. Subjects who were pregnant, those who had known renal, pituitary adrenal or terminal illness were excluded from the study.

The approval for this study was given by the Ethics Research Committee of the hospital. All the subjects who participated in the study gave informed written consent.

From each of the subjects, and with the aid of a questionnaire, we obtained demographic and anthropometric data. The aim of the study was explained to the subjects in our native language and English for those who could communicate in the later. The age, place of origin and domicile, and gender were obtained. Height and weight were measured, and BMI recorded as the ratio of weight/height^2 (kg/m^2).

Clear instructions were given to all the subjects on how to collect 24-hour urine sample. A day-time random spot urine sample and blood samples were collected at the end of the 24-hour urine sample collection. [9]

From the random spot urine samples collected, spot urine protein (SUP), spot urine creatinine (SUCr) and spot urine osmolality (SUOsm) were performed. Also from the 24-hour urine samples collected, 24-hour urine protein (24HUP), 24-hour urine creatinine (24HUCr) and 24-hour urine osmolality (24HUOsm) were performed. Hemoglobin (Hb) and serum creatinine were performed on the blood samples collected. Other tests done from the blood samples were HIV screening test, fasting serum lipid profile (FSLP) (total cholesterol, triglyceride (TG), high density lipoprotein cholesterol (HDL), low density lipoprotein cholesterol (LDL). Osmolality was determined by freezing point depression method using Precision Osmette 5002 osmometer, creatinine by modified Jeff's method and protein by photometric method. Creatinine clearance (ClCr) was determined. [9]

The potential predictors of urine creatinine studied were BMI, Hb, serum creatinine, SUOsm, SUP, 24HUV, 24HUP, 24HUOsm, serum cholesterol, serum TG, serum HDL, serum LDL and ClCr.

Statistical Analysis:

SPSS version 17.0 (SPSS Int. Chicago, II, USA) was used in analyzing the data. Descriptive statistics were used to determine the mean, minimum, maximum and range of values of SUCr and 24HUCr. The mean values of potential predictors of SUCr and 24HUCr were determined. The distribution and characterization of variables among subjects with different levels of 24HUCr were analyzed using cross-tabulation. Correlation statistics were used to determine the association of variables with SUCr on one hand, and 24HUCr on the other. Multivariate linear regression analyses were used to determine the strength of variables to predict urine creatinine. $P \leq 0.05$ was taken as statistically significant.

Definition of terms:

These were adopted from the terms used by Yeh et al. [7]

Normal urine creatinine: 24HUCr 300 – 3000mg.

Low urine creatinine or dilute urine: 24HUCr <300mg.

High urine creatinine or concentrated urine: 24HUCr >3000mg.

3. Results

The subjects studied were 136. Females constituted 72.1% and males 27.9%. The mean age of the subjects was 39±12 years. None of them has incomplete data or sample collection. As a result, there was no attrition. For all the subjects, the mean SUCr was 148±167, minimum value 14.7mg/dl, maximum value 746.7mg/dl and range of values 732.0mg/dl. The mean 24HUCr was 1203±316, minimum value 651.0mg, maximum value 2320mg, and range of values 1669.0mg. The mean values of other variables are shown in Table 1.

Table 1. *Characteristics of variables in Study subjects n=136.*

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,

All the subjects have 2HUCr in the normal range (300 – 3000mg). Consequently, the distribution and characterization of potential risk factors according to levels of urine creatinine were voided.

There was significant correlation between SUCr and BMI (r=0.225, p=0.009), SUP (r=0.292, p=0.001), SUOsm (r=0.223, p=0.009), 24HUP (r= -0.187, p=0.030), 24HUCr

(r= -0.178, p=0.038), serum creatinine (r= -0.212, p=0.013), serum cholesterol (r=0.246, p=0.004), serum LDL (r=0.282, p=0.001). Conversely, SUCr did not significantly correlate with Hb, 24HUV, 24HUOsm, serum TG, serum HDL, or ClCr (Table 2).

Table 2. *Correlation of Spot Urine Creatinine with selected variables in study subjects (n=136).*

Variables	Correlation coefficient(r)	P value
Body mass index	0.225	0.009
Hemoglobin	0.024	0782
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

Twenty four-hour urine protein significantly correlated with 24HUV (r=0.213, p=0.013), serum creatinine (r=0.741, p<0.001) and SUCr (r= -0.178, p<0.001). On the contrary, 24HUCr did not show significant correlation with BMI, Hb, SUP, SUOsm, 24HUP, 24HUOsm, serum cholesterol, serum TG, serum HDL or serum LDL (Table 3).

Table 3. *Correlation of 24-hour Urine Creatinine with selected variables in study subjects (n=136).*

Variables	Correlation coefficient(r)	P value
Body mass index	0.056	0.520
Hemoglobin	0.046	0593
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

The variables that predicted SUCr were SUP (p<0.001) and 24HUP (p=0.021), while BMI, serum creatinine, SUOsm, 24HUCr, serum cholesterol and LDL did not (Table 4).

Table 4. *Multivariate linear regression of variables with Spot Urine Creatinine in study subjects (n=136).*

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	-655.330 - -53.513
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.

Only one variable predicted 24HUCr - serum creatinine (p<0.001), while SUCr and 24HUV did not (Table 5).

Table 5. *Multivariate linear regression of variables with 24-hour Urine Creatinine in study subjects (n=136).*

Variables	Beta	T	P value	95% CI
Serum creatinine	0.723	26353	<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.

4. Discussion

This study showed that low and high urine creatinine were absent in the out-patient population as all of them have 24HUCr in the normal range (300 – 3000mg). Spot urine creatinine correlated significantly with BMI (r=0.225, p=0.009), SUP (r=0.292, p=0.001), SUOsm (r=0.223, p=0.009), 24HUP (r= -0.187, p=0.030), 24HUCr (r= -0.178, p=0.038), serum creatinine (r= -0.212, p=0.013), serum cholesterol (r=0.246, p=0.004), and serum LDL (r=0.282, p=0.001). Factors that significantly correlated with 24HUCr were 24HUV (r=0.213, p=0.013), serum creatinine (r=0.741, p<0.001), and SUCr (r= -0.178, p<0.001). Spot urine protein and 24HUP predicted SUCr, while only serum creatinine predicted 24HUCr.

In this study there was absence of low and high urine creatinine in subjects attending the general out-patient clinic. This disagrees with the prevalence, 8.1%, of low urine creatinine and 3.1% of high urine creatinine reported by Barr et al. [10] Their study was conducted in a US general population in contrast with ours that was done in a general out-patient clinic population in Nigeria. This difference in study design might have accounted for the observed differences between the two studies. In addition, our study subjects were patients who might have presented to hospital for one illness or the other that might impact on urine creatinine.

Our study showed that BMI was associated with SUCr but not with 24HUCr. This observation is similar to that reported in two studies. [10, 11] Two studies further demonstrated that BMI was a predictor of SUCr, [11, 12] in contrast with our study which showed that BMI did not predict SUCr and 24HUCr. Urine creatinine, a function of BMI, a measure of lean body mass, is dependent on muscle mass.

This study demonstrated that SUP and 24HUP were predictors of SUCr. This was slightly similar to a study that found protein intake associated with urine creatinine. [13] We observed that these two variables were not associated with 24HUCr. Protein in urine predicting SUCr, with 24HUCr in 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 SUCr 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. [14, 15]

There was an inverse correlation between SUCr and 24HUCr observed in this study. This implied that as SUCr increased, 24HUCr declined, and vice versa. Studies were sparse on the relationship between SUCr and 24HUCr.

The study showed that serum creatinine was associated with SUCr. Serum creatinine in normal state is maintained at a fairly 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. [16] However, elevated serum creatinine would be observed in impaired renal function, associated with reduced urine creatinine. [17] Expectedly, serum creatinine was a predictor of 24HUCr in this study.

Serum cholesterol and serum LDL were associated with SUCr, as observed in our study. Lipid abnormalities have been described in renal disease associated with reduced urine creatinine excretion. [18, 19] This might suggest that our study subjects might have renal impairment.

We noted that 24HUV was associated with 24HUCr in this study. A related study reported an association between 24HUV and ClCr. [20] In contrast, our study did not find any association between 24HUCr and ClCr. Nonetheless, urine volume tends to decrease with decreasing ClCr, and 24HUCr is a function of ClCr. This probably would explain the association between 24HUV and 24HUCr observed in this study.

5. Conclusion

Low and high urine creatinine were absent in subjects attending the general out-patient clinic. Proteinuric renal abnormalities, weight changes and dyslipidemia were common in these subjects with normal urine creatinine. There is need for clinicians to routinely conduct urine creatinine and further search for abnormalities of lipids, renal function and weight changes in subjects with normal urine creatinine attending the general out-patients clinics.

Limitations

Our study population was small. A larger sample size would have been better as it probably would have shown a proportion of those with low and high urine creatinine, however little they might be, and the potential risk factors of dilute and concentrated urine in this population.

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