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Albumin to Creatinine Ratio Is Fairly Correlated with Albumin Excretion Rate in Chronic Kidney Disease

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Abstract: Measurement of urine albumin excretion rate (AER) over a 24-h period is considered the gold standard technique for detecting albuminuria. However, the procedure is highly inconvenient for most patients. This study aimed to assess the accuracy of albumin to creatinine ratio in spot urine (UACR) as a surrogate to 24-h urine AER in patients with chronic kidney disease (CKD). This cross-sectional study included 92 patients with CKD (51 men and 41 women) admitted to Al-Basrah Teaching Hospital from January to October 2014. The 24-h AER was obtained using 24-h urine samples and the UACR was determined from a morning-void urine sample. Serum creatinine level was determined and general urine examination was performed using standard methods. Patients were divided into three groups according to glomerular filtration rate (GFR; ≥60, 30–59, and 15–29 mL/min/1.73 m^2). Pearson's correlation coefficients for ACR vs. 24-h AER were 0.609 ($P < 0.0001$) and 0.532 ($P < 0.0001$) for men and women, respectively. In the GFR groups, Pearson's correlation coefficients were, in the order listed above, 0.681 ($P = 0.0001$), 0.820 ($P = < 0.001$), 0.865 ($P = 0.002$) in men, and 0.721 ($P = 0.01$), 0.865 ($P = 0.002$), and 0.756 ($P = 0.04$) in women. In conclusion UACR determined using morning urine samples is fairley correlated with 24-h urine AER and is more practical and convenient for both the patient and the physician.

Keywords: Albuminuria, Chronic Kidney Disease, Diabetes Mellitus, Diabetic Nephropathy, Urine Sample

1. Introduction

The detection and quantification of proteinuria is crucial in the initial diagnosis and subsequent monitoring of renal diseases [1]. Proteinuria is recognized as an independent risk factor for cardiovascular disease. The degree of protein excreted in the urine varies with stress, exercise, hydration status, and posture, and is also affected by the diurnal cycle [2]. The gold standard test for proteinuria is quantitative estimation of albumin in urine collected over a 24-h period [3]. However, monitoring urine protein for 24 h a cumbersome and prone to errors, including incomplete collection, bacterial growth, incorrect timing, and incomplete bladder emptying, which requires hospital admission and inconvenience the patient, especially if repeated follow-up examinations are needed [4]. Collecting a morning urine sample for measuring urine albumin to creatinine ratio (UACR) is simple, and UACR has been found to be a powerful predictor of adverse renal and cardiovascular outcomes [5–7]. It has been found very useful as a screening test for nephropathy in diabetics [8] and hypertensives [9], and for predicting pre-eclampsia in early pregnancy [10]. According to the National Kidney Foundation – Kidney Dialysis Outcomes Quality Initiative (NKF-KDOQI) guidelines, an albumin excretion rate (AER) threshold of ≥30 mg/24 h sustained for >3 months indicates chronic kidney disease (CKD). This value is approximately equivalent to a UACR in a morning untimed urine sample of ≥30 mg/g or ≥3 mg/mmol [11]. A UACR of 2.5–25 mg/mmol in men and 3.5–35 mg/mmol in women indicates microalbuminuria, while a UACR of >25 mg/mmol in men and >35 mg/mmol for women indicates macroalbuminuria [5]. Several studies support the use of UACR instead of 24-h urinary AER [12–15]. Some recent guidelines, e.g., those by the NKF (USA), recommend the examination of morning UACR for the detection of proteinuria [15]. Considering this, morning UACR testing may be an easy alternative for measuring urine albumin (UA) level. However, some practicing physicians

are concerned that spot morning UACR testing may not yield accurate results if the glomerular filtration rate (GFR) is severely compromised [16]. With the above in mind, the aim of this study was to compare UACR to 24-h urinary AER values at various stages of CKD and to determine whether UACR can replace AER in clinical practice in our community.

2. Patients and Methods

This cross-sectional study included 92 patients (51 [55.44%] men and 41 [44.56%] women) with CKD who were randomly selected from the medical wards of Basrah Teaching Hospital from January to October 2014. Patient age ranged from 21 and 84 years for men and 40 and 85 years for women (mean: 61.239 ± 14.604). The 24-h urine samples were collected from 8 am on the first day and until 8 am on the second day. The first sample obtained on the first day was excluded from the analysis. The collected urine was analyzed using the albumin-in-urine assay from Randox (an immunoassay for the latex agglutination reaction). The normal 24-h UA level is <30 mg/24 h according to the NKF-KDOQI guidelines [12, 17, 18]. The spot morning urine sample for ACR calculation was obtained before starting the 24-h collection. Samples were processed as early as possible after collection. Morning urine samples were evaluated for creatinine using the assay from BioCheck [19]. The normal value of UACR is <2.5 mg/mmol (<25 mg/g) for men and <3.5 mg/mmol (<35 mg/g) for women. Blood tests (blood urea, serum creatinine, fasting blood glucose, hemoglobin %) and urinalysis were performed. We determined body weight and eGFR (in mL/min/1.73 m^2) for all patients. GFR was calculated using the Modification of Diet in Renal Disease study equation [15], and all patients were divided into three groups according to CKD stage (depending on GFR). The inclusion criteria were GFR >15 mL/min/1.73 m^2, diabetes mellitus, hypertension, cardiovascular disease, structural renal tract disease, multiple renal calculi or prostatic hypertrophy, and systemic diseases with potential kidney involvement, e.g., systemic lupus erythematosus, family history of CKD, or hereditary kidney disease. The exclusion criteria were urinary tract infection identified by urinalysis, existing congestive cardiac failure (previous echocardiography), acute febrile illness, heavy exercise within 24 h, menstruation or vaginal discharge, drug administration (especially non-steroidal anti-inflammatory drugs, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers), pregnancy, need for urgent dialysis, and GFR <15 mL/min/1.73 m^2.

Statistical analysis: Data were analyzed using the Statistical Package for the Social Sciences (SPSS), version 20.0. Associations between UACR (all patients, normal UACR, and abnormal UACR) and risk factors were compared with associations between 24-h UA (all patients, normal 24-h UA, and abnormal 24-h UA) and risk factors. Pearson's correlation coefficients were used to test for correlations between UACR and 24-h UA in men and women separately. The independent sample t-test was used to detect statistically significant differences between UACR and 24-h UA depending on the patient's condition. Descriptive statistics were used to determine the mean values of UACR and 24-h UA at each stage of CKD. A P-value < 0.05 was considered statistically significant.

3. Results

Patient characteristics are shown in Table 1. Out of the 51 men, 32 (62.7%) had diabetes, 26 (51%) had hypertension, and 25 (49%) had other comorbidities such as ischemic heart disease, rheumatoid arthritis, systemic lupus erythematosus, and so on. Out of the 41 women, 26 (63.4%) had diabetes, 23 (56.1%) had hypertension, and 28 (68.3%) had other comorbidities.

Table 1. *Characteristics of the study population.*

Characteristics		All patients (N = 92)	Men (N = 51)	Women (N = 41)
Age (years; mean ± SD)		61.24 ± 14.604	63.78 ± 14.889	58.07 ± 13.768
Diabetes mellitus		58 (63%)	32 (62.7%)	26 (63.4%)
Hypertension		49 (53.3%)	26 (50.9%)	23 (59.1%)
Other disease		53 (57.6%)	25 (49.1%)	28 (68.3%)
GFR, mL/min/1.73 m^2		41.94 ± 22.288	46.01 ± 23.193	36.88 ± 20.257
CKD stage	1 + 2	17 (18.47%)	11 (21.6%)	6 (14.6%)
	3	47 (51.1%)	30 (58.8%)	17 (41.5%)
	4	28 (30.43%)	10 (19.6%)	18 (43.9%)
UACR (mg/mmol)		3.61 ± 1.02	3.14 ± 0.74	4.2 ± 1.03
24-h UA (g/24 h)		0.64 ± 0.722	0.5 ± 0.4	0.82 ± 0.97
Serum creatinine (mg/dL)		1.93 ± 0.798	1.94 ± 0.8001	1.92 ± 0.804

CKD: chronic kidney disease, GFR: glomerular filtration rate, UA: urine albumin, UACR: urine albumin to creatinine ratio

Forty-one (80.4%) men had a UACR > 25 mg/g. Of these, 32 (78%) had comorbidities, while nine (22%) did not have systemic disease. In comparison, among the 10 (19.6%) patients with a UACR < 25 mg/g, the corresponding patient numbers were two (20%) and eight (80%), respectively. Also 31 (60.7%) male had 24h UA>0.3g, 22 (70.9%) of them with, and 9 (29.1%) without systemic disease; whereas 20 (39.3%) male had 24h UA<0.3g, 11 (55%) with, and 9 (45%) without systemic disease. A significant difference was found in UACR and 24h UA between males with and without comorbidities (P < 0.0001) (Table 2)

Table 2. *Mean values of urine albumin to creatinine ratio (UACR) and 24-h urine albumin (UA) according to comorbidities in men.*

		No.	Mean UACR	Comorbidities			P- value
				Status	No	Mean	
ACR (mg/mmol)	>2.5	41	3.38 ± 0.61	Present	32	3.6 ± 0.51	<0.0001
				Absent	9	2.74 ± 0.1	
	<2.5	10	2.18 ± 0.39	Present	2	2.11 ± 0.00	
				Absent	8	2.04 ± 0.04	
24h UA (g/24 h)	>0.3	31	0.7 ± 0.4	Present	22	0.82 ± 0.41	<0.0001
				Absent	9	0.4 ± 0.1	
	<0.3	20	0.2 ± 0.05	Present	11	0.25 ± 0.04	
				Absent	9	0.2 ± 0.04	

Thirty-one (75.6%) women had a UACR > 3.5 mg/g, of which 22 (70.9%) had systemic disease and nine (29.1%) did not. Among the 10 (24.4%) women with a UACR < 2.5 mg/g, two (20%) and eight (80%), respectively, had and did not have systemic disease. In comparison, 30 (73.2%) women had a 24-h UA > 0.3 g/24 h; and systemic disease was present in 21 (70%) and absent in nine (30%). Among the 11 (26.8%) women with a 24-h UA < 0.3 g/24 h, three (27.2%) had systemic disease and eight (72.7%) did not. A significant difference was found in UACR and 24-h UA between women with and without comorbidities (P < 0.0001) (Table 3).

Table 3. *Mean values of urine albumin to creatinine ratio (UACR) and 24-h urine albumin (UA) according to comorbidities in women.*

		No.	Mean UACR	Comorbidities			P - value
				Status	No	Mean	
ACR (mg/mmol)	>3.5 (mg/mmol)	31	4.6 ± 0.8	Present	22	4.4 ± 0.36	<0.0001
				Absent	9	3.71 ± 0.11	
	<3.5 (mg/mmol)	10	2.8 ± 0.35	Present	2	3.05 ± 0.1	
				Absent	8	2.05 ± 0.06	
24h UA (g/24 h)	>0.3g/24h	30	1.14 ± 1.05	Present	21	1.05 ± 0.3	<0.0001
				Absent	9	0.5 ± 0.13	
	<0.3g/24h	11	0.2 ± 0.06	Present	6	0.23 ± 0.03	
				Absent	8	0.2 ± 0.03	

The correlation between UACR and 24-h UA in patients with established and advanced CKD is shown in Table 4. For stage 2 (GFR ≥ 60 mL/min/1.73 m^2), the *r* values were 0.681 and 0.721 for men and women, respectively. For stage 3 (GFR = 30–59 mL/min/1.73 m^2), the corresponding *r* values were 0.820 and 0.865, whereas for stage 4 (GFR = 15–29 mL/min/1.73 m^2) they were 0.685 and 0.756. All of these correlations were highly statistically significant. There was a significant correlation between total UACR and total 24-h UA (Table 4).

Table 4. *Correlations between urine albumin to creatinine ratio (UACR) and 24-h urine albumin (UA) for the different glomerular filtration rate (GFR) groups.*

GFR	Sex	No.	UACR	24-h UA	*R*	P- value
≥60	Male	6	3.4 ± 0.65	0.83 ± 0.3	0.681	0.001
	Female	11	2.23 ± 0.31	0.3 ± 0.12	0.721	0.01
30–59	Male	17	3.91 ± 1.21	0.63 ± 0.8	0.820	<0.001
	Female	30	3.28 ± 0.6	0.51 ± 0.44	0.865	0.002
15–29	Male	18	4.7 ± 0.64	1.15 ± 1.15	0.685	0.002
	Female	10	3.92 ± 0.5	0.71 ± 0.24	0.756	0.04
Total	Male	51	3.14 ± 0.74	0.5 ± 0.4	0.609	<0.0001
	Female	41	4.2 ± 1.03	0.82 ± 0.97	0.532	<0.0001

4. Discussion

This study found a significant correlation between UACR and 24-h UA level both in men (P < 0.0001, correlation coefficient *r* = 0.609) and women (P < 0.0001, *r* = 0.532) in patients with CKD. These findings agree with the conclusions of previous studies, suggesting that the use of UACR is appropriate for the quantitative assessment of UA level and can be used instead of 24-h UA level [5, 7, 11, 12]. In patients with diabetes, albumin excreted in the urine should be used because it is a surrogate end-point for early diabetic nephropathy [13]. However, the study by Gatling *et al*. has showed that, for both type 1 and type 2 diabetes, UACR estimated using an overnight urine sample has greater sensitivity (96%) and specificity (100%) than UACR obtained using a morning urine sample (sensitivity: 80%, specificity: 81%) [20]. Moreover, albumin level in urine is more sensitive than protein in urine for detecting CKD. For example, a cross-sectional study of the general population found that 67.5% of patients with albumin in their urine had no detectable protein in their urine, whereas 8% of subjects with protein in urine had no albumin in urine (especially in patients without diabetes). Thus, if protein in the urine is measured, as many as 67.5% of patients with albumin in their urine may be missed [5]. The value of UA obtained from a

first morning void correlates better with 24-h UA than the UA value obtained from random spot urine samples because the former is less influenced by factors such as physical exercise and diet [21, 22]. UACR is more useful in diagnosing microalbuminuria and monitoring albumin in the urine over time. On this basis, measuring UACR in a first morning void is recommended when determination of 24-h UA is not feasible. Additionally, UACR is easy to determine and generally accurate, with a minimal number of false-negative results [23]. Finally, in a cohort of 92 patients, this study identified a strong correlation between UACR values in morning spot urine samples and 24-h UA at different levels of GFR both in men and women, with P-values indicating statistical significance. These correlations were significant for each level of GFR, corroborating the findings of the NKF [15, 17–19].

5. Conclusion

This study found that in patients with CKD; UACR determined from a spot morning void is a simple and reliable surrogate for 24-h UA, and can be used to quantify albumin in the urine without the need for timed urine collection. Although the correlations between total UACR and total 24h UA in male and female were fair, there were strong correlations when individual stages of CKD considered.

Conflict of Interest

The authors declare that they have no conflict of interest.

Ethical Approval

The study was approved by the ethical committee in Basrah medical college. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

References

[1] Burtis C, Ashwood E, Bruns D (2008) Tietz text book of clinical chemistry and molecular diagnosis, 4th edn. Elsevier, Missouri, USA, pp 822, 1241–1245, 1687–1694.

[2] Rowe DJ, Bagga H, Betts PB (2009) Normal variations in rate of albumin excretion and albumin to creatinine ratios in overnight and daytime urine collections in non-diabetic children. Br Med J (Clin Res Ed) 291: 693–694.

[3] Côté AM, Firoz T, Mattman A, Lam EM, von Dadelszen P, Magee LA (2008) The 24-hour urine collection: Gold standard or historical practice? Am J Obstet Gynecol 199: 625. e1-6.

[4] Newman DJ, Pugia MJ, Lott JA, Wallace JF, Hiar AM (2000) Urinary protein and albumin excretion corrected by creatinine and specific gravity. Clin Chim Acta 294: 139–155.

[5] Chronic Kidney Disease Prognosis Consortium, Matsushita K, van der Velde M, Astor BC, Woodward M, Levey AS, de Jong PE, Coresh J, Gansevoort RT (2010) Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: A collaborative meta-analysis. Lancet 375: 2073–2081.

[6] Hemmelgarn BR, Manns BJ, Lloyd A, James MT, Klarenbach S, Quinn RR, Wiebe N, Tonelli M; Alberta Kidney Disease Network (2010) Relation between kidney function, proteinuria, and adverse outcomes. JAMA 303: 423–429.

[7] Ruggenenti P, Gaspari F, Perna A, Remuzzi G (1998) Cross sectional longitudinal study of spot morning urine protein: creatinine ratio, 24-hour urine protein excretion rate, glomerular filtration rate, and end stage renal failure in chronic renal disease in patients with diabetes. BMJ 316: 504–509.

[8] Looker H, Nelson R. Reading the three leaves- how to enrich clinical trials of diabetic kidney disease. Kidney International 2017, vol 92, Iss 1, p23-5.

[9] Akif A, Arsalan M, Hasan S, Sana A, Aquil A. Protein Creatinine Index: An Alternative for Screening Nephropathy in Hypertensives. J Clin Diag Res 2018, vol 12, Issue 3, p15-18.

[10] Mishra V, Goyal P, Priyankur R, Choudhary S, Aggarwal R, Gandhi K, et al. evaluation of spot urinary albumin-creatinine ratio as screening tool in pre-eclampsia in early pregnancy. J Obst Gyn India 2017. Vol 67, iss 6, pp 405-8.

[11] Johnson D, Caring for Australians with Renal Impairment (CARI) (2005) The CARI guidelines: Evaluation of renal function. Nephrology (Carlton) 10 Suppl 4: S133–S176.

[12] Ng WY, Lui KF, Thai AC (2000) Evaluation of a rapid screening test for microalbuminuria with a spot measurement of urine albumin-creatinine ratio. Ann Acad Med Singapore 29: 62–65.

[13] Incerti J, Zelmanovitz T, Camargo JL, Gross JL, de Azevedo MJ (2005) Evaluation of tests for microalbuminuria screening in patients with diabetes. Nephrol Dial Transplant 20: 2402–2407.

[14] National Kidney Foundation. (2002) K/DOQI clinical practice guidelines for chronic kidney disease: Evaluation, classification, and stratification. Am J Kidney Dis 39 (2 Suppl 1): S1–S266.

[15] Kidney Disease Outcomes Quality Initiative (K/DOQI) (2004) K/DOQI clinical practice guidelines on hypertension and antihypertensive agents in chronic kidney disease. Am J Kidney Dis 43 (5 Suppl 1): S1–S290.

[16] Han JH, Kim KS, Yoon JY (2007). The enhanced diffusional mixing for latex immunoagglutination assay in a microfluidic device. Anal Chim Acta 584: 252–259.

[17] Eknoyan G, Hostetter T, Bakris GL, Hebert L, Levey AS, Parving HH, Stefes MW, Toto R (2003) Proteinuria and other markers of chronic kidney disease: A position statement of the national kidney foundation (NKF) and the national institute of diabetes and digestive and kidney diseases (NIDDK). Am J Kidney Dis 42: 617–622.

[18] Jafar TH, Chaturvedi N, Hatcher J, Levey AS (2007) Use of albumin creatinine ratio and urine albumin concentration as a screening test for albuminuria in an Indo-Asian population. Nephrol Dial Transplant 22: 2194–2200.

[19] Mattix HJ, Hsu CY, Shaykevich S, Curhan G (2002) Use of albumin/ creatinine ratio to detect microalbuminuria: Implication of sex and race. J Am Soc Nephrol 13: 1034–1039.

[20] Gatling W, Knight C, Mullee MA, Hill RD (1988) Microalbuminuria in diabetes: A population study of the prevalence and an assessment of three screening tests. Diabet Med 5: 343–347.

[21] American Diabetes Association (2007) Standards of medical care in diabetes -- 2007. Diabetes Care 30 [Suppl 1]: S4–S41.

[22] Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, et al. (2003) Seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. Hypertension 42: 1206–1252.

[23] Miller WG, Bruns DE, Hortin GL, Sandberg S, Aakre KM, McQueen MJ, et al. (2009) Current issues in measurement and reporting of urinary albumin excretion. Clin Chem 55: 24–38.