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Performance Evaluation of Semi-quantitative Urine Albumin Creatinine Ratio Using Meditape UC-11A Strip Test

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ABSTRACT

The Urine Albumin/Creatinine Ratio (uACR) is one of the earliest markers of glomerular disorders. A comparative study of semi-quantitative urine uACR and quantitative uACR tests was carried out using Meditape UC-11A test strips on the SysmexUC-3500 (automated urinalysis instrument) and Roche Cobas 501, respectively. A total of 213 retrospective data of urine chemistry tests were collected. Semi-quantitative urine albumin, creatinine, and uACR data were obtained using Meditape UC-11A strips on SysmexUC-3500, where as quantitative data were obtained using Roche Cobas c501. A weighted Cohen's Kappa agreement, sensitivity, specificity, PPV, NPV, and accuracy were analyzed using data from both instruments. The Kappa values for urine albumin, creatinine, and uACR between the semi-quantitative and quantitative methods were 0.83 (CI 0.771–0.880), 0.535(CI0.417–0.652), and 0.691(CI0.606–0.775), respectively. The sensitivity, specificity, PPV,NPV, and accuracy of semi-quantitative methods were 90%, 73.3%, 75%, 89.2%, and 81.2%, respectively. The semi-quantitative uACR test on the UC-3500 showed excellent performance and could be used as a screening test for early detection of impaired kidney function.

Keywords: uACR, CKD, albuminuria

INTRODUCTION

Proteinuria is a fundamental clinical indicator of glomerular damage.[1] Since albumin constitutes the primary component of proteinuria in most kidney disorders, the clinical terminology tends to shift towards "albuminuria." Moreover, recent epidemiological data has raised concerns about albuminuria due to its strong association with the risk of kidney and cardiovascular diseases. The latest 2012 Kidney Disease Improving Global Outcomes (KDIGO) recommendation has listed albuminuria as an essential marker for stratifying the severity of chronic kidney disease.[2] Additionally, albuminuria is one of the earliest markers of glomerular disorders, including renal impairment in diabetes, often detectable before a decline in kidney function as indicated by the Estimated Glomerular Filtration Rate (eGFR) value.

The gold standard for evaluating albuminuria and proteinuria is measuring their excretion rates in the urine within 24 hours, referred to as the Albumin Excretion Rate (AER) and Protein Excretion Rate (PER), respectively. However, this test is rarely conducted due to its time-consuming and labor-intensive nature. Moreover, the method is associated with reduced accuracy and susceptibility to errors during sample collection procedures.[3] As a result, the quantitative determination of urine albumin levels typically relies on immunological tests using the turbidimetric method. Meanwhile, urine creatinine levels are commonly measured quantitatively by clinical chemistry tests using the enzymatic Jaffe method.[2] The albumin level is then compared with the urine creatinine level as a ratio known as the Urine Albumin/Creatinine Ratio (uACR). Never the less, it is worth noting that the availability of quantitative tests is limited, and the associated expenses can be considerable.

KDIGO has addressed the significance of an AER of ≥30 mg/24 hours, persisting for more than three months as an indication of chronic kidney disease.[2] Research has demonstrated that this value is equivalent to an uACR of ≥30 mg/g in random urine samples. Ameta-analysis study conducted by the CKD Prognosis Consortium also established a correlation between uACR levels and the risk of mortality and disease progression in general and cardiovascular disease risk populations. Consequently, KDIGO has recommended the measurement of urine uACR as the primary method for investigating albuminuria.[2,4-6]

Urine albumin and creatinine tests are available as dipsticks, such as the Sysmex Meditape UC-11A and Meditape UC-12S, which provide semi-quantitative

uACR values. Combined with the automated color sensor reading through reflectance photometry on the Sysmex UC-3500 instrument, this semi-quantitative uACR test demonstrates excellent analytical and diagnostic performance, particularly for chronic kidney disease screening.[7,8] The objective of this study was to determine the concordance, sensitivity, specificity, Negative Predictive Value (NPV), and Positive Predictive Value (PPV) of the urine uACR parameter between the semi-quantitative uACR measurement using Meditape UC-11A and those obtained using quantitative methods.

METHODS

The study was conducted retrospectively, using secondary data from 213 urine samples at the Clinical Pathology Laboratory of Eka BSD Hospital, Banten, Indonesia, collected from patients who underwent medical check-ups between November 2021 and June 2022. The uACR values were measured semi-quantitatively using Meditape UC-11A on Sysmex UC-3500 and quantitatively with Roche Cobas c501. The urine samples used in this study were midstream morning urine samples. Samples were analyzed promptly on both instruments in less than 2 hours after sample collection, in accordance with laboratory standard procedures.

Data were retrieved through the HCLAB Laboratory Information System (LIS) at the Eka BSD Hospital Clinical Pathology Laboratory, following approval from the laboratory chief. Gender, age, albumin, creatinine, and uACR values were collected, but patient identifiers such as name and medical record number were excluded. All data were compiled in case report forms under the supervision of the principal investigator. Ethical clearance for this study was obtained from Atma Jaya University with reference number 16/10/KEP-FKIKUAJ/2022.

Urine albumin, creatinine, and uACR tests were conducted semi-quantitatively using Meditape UC-11A strips and analyzed with the Sysmex UC-3500. The urine albumin measurement test principle relies on the reaction of tetrabromophenolblue with albumin. Meanwhile, creatinine was measured using the Benedict-Behre method. Using this method, creatinine was reacted with 3,5-dinitrobenzene, hydrogen peroxide was released, and the color indicator was changed on the dipstick pad. This test is an alternative method to the Jaffe method and is considered to have less glucose interference. However, it may give lower results in urine containing ketone within a particular concentration.[9,10] The albumin concentration was the n categorized into five levels: 10, 30, 80, 150, and >150 mg/L, while the creatinine concentration was categorized as 10, 50, 100, 200, and 300 mg/dL. On the other hand, the quantitative urine albumin, creatinine, and uACR were measured with the Roche Cobas c501 instrument. Albumin levels were measured using the turbidimetric immuno assay method, whereas urine creatinine levels were measured using the enzymatic method.

The semi-quantitative uACR value was automatically calculated according to the instrument's settings. The results were classified into the following categories: "diluted,""normal," 1+ (30, 80, or 150 mg/g), ≥1+ (≥ 80 or ≥ 150 mg/g), or 2+ (≥ 300 mg/g). A diluted uACR result indicated that the sample was too diluted to calculate the uACR accurately, and it was subsequently excluded from the study.

Data processing and analysis were performed using IBMSPSS Statistics for Windows, Version 20.0 (IBM Corporation, New York, USA), and Microsoft Excel. The Kolmogorov-Smirnov test was employed to assess the data's normality. Subsequently, the agreement between the semi-quantitative and quantitative methods for the urine albumin, creatinine, and uACR levels was evaluated through the weighted Cohen's Kappa with linear weighting.

The urine albumin data were categorized as <30 mg/L, 30-150 mg/L, and>150 mg/L. The urine creatinine data were categorized into <50 mg/dL, 50-200mg/dL, and >200 mg/dL. The urine uACR results were classified into three groups: <30 mg/g; 30-300 mg/g, and >300 mg/g. To evaluate the diagnostic performance of the semi-quantitative uACR test to detect normal (<30 mg/g) or abnormal (≥ 30 mg/g) uACR levels, the sensitivity, specificity, PPV, NPV, and accuracy were determined. The quantitative uACR method was used as the reference method for this analysis.

RESULTS AND DISCUSSIONS

Two hundred thirteen subjects were involved, comprising 118 males and 95 females. The median age was 57, with an age range of 27 to 84. Of the 213 subjects, 43 were identified as diluted and consequently excluded from the uACR analysis. Therefore, only 170 subjects had complete data for uACR determination using quantitative and semi-quantitative methods.

The semi-quantitative and quantitative urine albumin data were categorized as <30mg/L, 30-150 mg/L, and >150 mg/L, as shown in Table 1. The analysis yielded a weighted Kappa value of 0.830(CI0.771–0.888) with a p-value<0.001, indicating a robustagreement between the semi-quantitative method and the quantitative method of albumin determination.

Table1. Agreement between urine albumin levels determined by semi-quantitative and quantitative methods

		Quantitative Albumin (mg/L)			Total
		<30	30–150	>150	
Semi-quantitative (mg/L) albumin	<30	111	3	1	115
	30–150	11	36	13	60
	>150	0	1	37	38
Total		122	40	51	213

Weighted Kappa 0.830 (CI0.771– 0.888), p - value<0.001

Table 2. Agreement between urine creatinine levels determined by semi-quantitative and quantitative methods

		Quantitative Creatinine (mg/dL)			Total
		<50	50-200	>200	
Semi-quantitative creatinine (mg/dL)	<50	34	16	1	51
	50-200	14	133	12	159
	>200	0	0	3	3
Total		48	149	16	213

Weighted Kappa 0.535 (CI0.417–0.652), p-value <0.001

Table 3. Agreement between uACR levels determined by semi-quantitative and quantitativemethods

		Quantitative uACR (mg/g)			Total
		<30	30–300	>300	
Semi-quantitative uACR(mg/g)	<30	66	8	0	74
	30–300	23	28	2	53
	>300	1	10	32	43
Total		90	46	34	170

Weighted Kappa 0.691 (CI0.606 – 0.775), p-value <0.001

Similarly, the urine creatinine data from both instruments were grouped into three categories such as <50mg/dL, 50-200 mg/dL, and >200 mg/dL, as shown in Table 2. Subsequently, a weighted Kappa value of 0.535 (CI 0.417 – 0.652) with a p-value <0.001 was obtained, indicating a moderate agreement between the semi-quantitative method and the quantitative method of urine creatinine examinations.

Moreover, the urine uACR data were divided into groups based on the uACR levels:<30 mg/g), 30-300 mg/g, and >300 mg/g. The distribution of results is presented in Table 3. A weighted Kappa value of 0.691(CI0.606–0.775) with a p-value <0.001 was obtained, indicating a substantial agreement between the semi-quantitative and quantitative methods of urine uACR measurement.

Table 4 presents the diagnostic performance of semi-quantitative uACR measurement to identify abnormal uACR levels. According to the KDIGO 2012 guideline, a uACR cut-off of ≥30 mg/g was used to determine the diagnosis of kidney function impairment.[2] The results demonstrated excellent diagnostic performance, with the sensitivity, specificity, PPV, NPV, and accuracy values of the semi-quantitative uACR test of 90%, 73.3%, 75%, 89.2%, and 81.2%, respectively.

Table 4. Agreement between uACR levels determined by semi-quantitative and quantitative methods

		Quantitative uACR		Total
		Positive(≥30 mg/g)	Negative(<30 mg/g)	
Semi-quantitative uACR	Positive (≥30 mg/g)	72	24	96
	Negative (<30 mg/g)	8	66	74
	Total	80	90	170

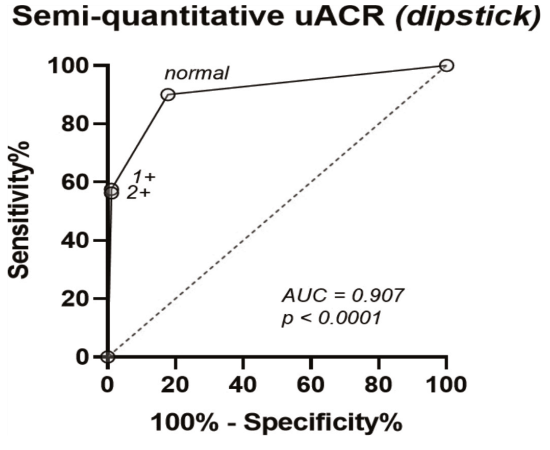

Figure 1. ROC curve of the diagnostic performance of semi-quantitative uACR with quantitative methods as reference method

Furthermore, a Receiver Operating Characteristic (ROC) curve was generated, as depicted in Figure 1. With a cut-off of uACR ≥30 mg/g,semi-quantitative uACR measurements using strips showed an area Under the Curve (AUC) of the ROC curve with a value of 0.907. The best performance was demonstrated when using the uACR "normal" or"<30 mg/g"category as the cut-off, with a sensitivity and specificity of 90.0% and 82.2%, respectively. These findings were consistent with the manufacturer's recommendation.

This study strongly agreed between semi-quantitative on Sysmex Meditape UC-11A and quantitative uACR and albumin measured on Roche Cobas c501. This finding showed better agreement than the previous report by Shinae *et al.*[11] The disparity between this study's results and the previously published data might be attributed to differences in the instruments and examination methods.

It was also found that the diagnostic performance of the semi-quantitative uACR was excellent, with notably high sensitivity and accuracy. These results suggested that the semi-quantitative method might be suitable for screening impaired kidney function. With a high NPV, a semi-quantitative uACR test could be used as an exclusion test for impaired renal function. This test might reduce the number of unnecessary quantitative tests. Consequently, it might help clinicians and laboratories increase efficiency, especially in managing diabetic nephropathy, which requires regular monitoring.[12] This finding was in accordance with research by Currin *et al*. that demonstrated that asimple uACR test with good NPV could be used in albuminuria screening in primary care or limited-resources facilities.[13]

However, it is essential to note that adequate samples with creatinine >200 mg/dL were not obtained in this study, which might contribute to the low Kappa value for this parameter. Therefore, obtaining a sufficiently large sample size for each group could be an area of improvement for future research. Moreover, acost-efficiency analysis to prove the efficiency of the semi-quantitative uACR test compared to quantitative methods is also an interesting topic to be discussed further. The analysis may be used to formulate the most effective algorithm for utilizing semi-quantitative uACR examination.

CONCLUSIONS AND SUGGESTIONS

Based on this study's findings, the semi-quantitative uACR test using the Meditape UC-11A strip on the SysmexUC-3500 is a suitable screening test for detecting impaired kidney function. The semi-quantitative method demonstrated high sensitivity and specificity and a good correlation with the quantitative method. This finding offers a more cost-effective alternative for screening impaired renal function, as the semi-quantitative method is cheaper than the quantitative method.

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