

Correlation of Urinary Protein Creatinine Ratio with 24-Hour Urinary Protein in Indian Patients

Kamakshi Narula¹, Sanjeev K. Verma², Shahbaj Ahmad³

¹Senior Resident, ²Professor, ³DNB (Nephrology), Assistant Professor, Department of General Medicine. Himalayan Institute of Medical Sciences, SRHU Dehradun - 248 016.

Corresponding Author: Shahbaj Ahmad

ABSTRACT

Background: 24-hour urinary protein (24-UP) is the gold standard for the assessment of proteinuria, but urine collection is tedious and prone to error. So spot urinary protein creatinine ratio (UPCR) is used as a surrogate for 24-UP. There are only a few studies which have validated the correlation between UPCR with 24-UP in Indian population.

Aims: To assess the correlation between UPCR with 24-UP in Indian patients.

Settings and Design: Cross sectional study in a tertiary teaching health centre.

Methods: The study was of one-year duration, which included adult patients with dip stick positive proteinuria. The patients with uncontrolled hypertension or diabetes, febrile illness, raised serum creatinine, pregnancy or during the menstrual period were excluded. All the patients collected 24-hour urine samples on a normal diet and routine daily activity. Following day the patient submitted the can of 24-hour urine & a separate container with freshly voided urine.

Statistical analysis used: Mean, standard deviation & Pearson's correlation coefficient.

Results: Out of 112 patients, only 100 samples were included for final analysis. The mean age of the finally included 100 patients was 53.3 years, of which 68% were male. The mean 24-UP & UPCR were 3200.58 ± 2969.66 & 3.12, respectively. Pearson's correlation coefficient between UPCR & 24-UP was 0.78. The relationship was stronger at a lower level of proteinuria.

Conclusions: UPCR shows a good correlation with 24-UP in the Indian patients, and can be used as a surrogate for timed urine collection for proteinuria.

Keywords: 24-hour urinary protein, Dipstick, Indian patients, Proteinuria, UPCR, Urinary creatinine, Urinary protein.

INTRODUCTION

Proteinuria is an important hallmark of kidney disease. [1] It has both diagnostic and prognostic value. Proteinuria indicates glomerular involvement in the disease process. The diseases like HTN, SLE, [2,3] preeclampsia, [4] IgA nephropathy [5,6] with a significant amount of proteinuria has a worse outcome compared to the non-proteinuric patient. [7]

The assessment of proteinuria is often used as a screening test for kidney diseases. The gold standard for the assessment of proteinuria is the measurement of 24-hour urinary protein. [8] For this measurement, the patient needs to collect 24-hours urine. Therefore, this measurement is time-consuming, tedious and not readily available during the first contact with the physician. To circumvent the problem of 24-hour urinary collection spot urinary protein creatinine ratio is estimated. One of the determinants of protein and creatinine excretion in urine is the race of the person. [9] There are only a few studies which have validated UPCR in Indian population. [10,11]

So, we aimed to assess the relationship between UPCR and 24-hour urinary protein in the patient having dip-stick proteinuria.

MATERIAL & METHOD

This was a cross-sectional study carried out at a tertiary teaching hospital in Dehradun from July 2014 to June 2015 after obtaining permission from the IRB. The patients were included by convenient sampling method. The patient aged > 18 years of age, found to have dip stick proteinuria on the OPD basis, and the physician felt the need to quantitate the amount of proteinuria were eligible for enrollment in the study. The exclusion criteria were pregnancy, menstrual period, high-grade fever, evidence of urinary tract infection, uncontrolled diabetes mellitus or hypertension or raised serum creatinine (>1.2mg/dl).

The patients were explained to collect 24 -hour urine in the cane starting from the morning of the day before the scheduled day of the visit. No specific instruction was given to the patient regarding dietary intake, amount of fluid intake or physical activity. The urine samples were collected without adding any preservative. On arrival to the hospital, the patient submitted spot urine also. The samples were processed the same day for proteinuria and urinary creatinine. 24-hour urinary protein and spot urinary protein creatinine ratio were derived from these values.

Method of urinary creatinine & protein estimation: Urine creatinine was measured by the alkaline picrate kinetic method & urine protein by turbidimetry. All assays were performed, strictly adhering to standard operating procedures.

Statistical analysis: For the sample size calculation, we assumed the correlation coefficient between UPCR and 24-hour urinary protein to be 0.30. Sample size of 92 patients was required for this correlation to be significantly different for α -level of 0.05 and for β -level 0.10 (power 90%). Mean & standard deviations were used to summarise the interval data. The Pearson correlation coefficient was used to find the association

between Urine protein creatinine ratio and 24-hours urinary protein. $P < 0.05$ was considered statistically significant.

RESULTS

During the study period of one 112 patients were included out of which 12 patients (10%) were excluded because of protocol violation, i.e. an improper collection of urine samples. So, only 100 patients were included for final analysis. The age of the study patients was 53.3 ± 11.5 years (mean \pm SD), and 68% of patients were male (Table I).

Table I: Baseline characteristics of the patients

Characteristics	Value (N = 100)
Age, years (mean \pm SD)	53.31 \pm 11.51
Male	68
Body mass index, Kg m^{-2} (mean \pm SD)	23.00 \pm 1.92
Etiological factors	
T2DM	38%
HTN	19%
T2DM + HTN	30%
Others: SLE, rheumatological disorders, primary glomerular diseases	13%

Diabetes was the leading cause of proteinuria, followed by hypertension. A small number (13%) of the patients had SLE, primary glomerular disease and other rheumatological diseases. The mean 24-hour urinary protein was 3200.58 ± 2969.66 mg with the range being 200 mg to 14300 mg (Table II).

Table II: 24-hour urinary protein distribution among the patients.

Proteinuria (mg/24 hours)	No. of the patients (N = 100)
>150 - 300	7
>300 - 500	8
>500 - 1000	13
>1000 - 3500	37
>3500 - 5000	9
>5000	26
Mean \pm SD	3200.58 \pm 2969.66
Range	200 - 14300

In our study, 93% of patients had macroscopic proteinuria with 35% of the patients excreting more than 3.5 g protein in 24 hours and only 7% less than 300mg. Similarly, mean urine protein creatinine ratio was 3.12.

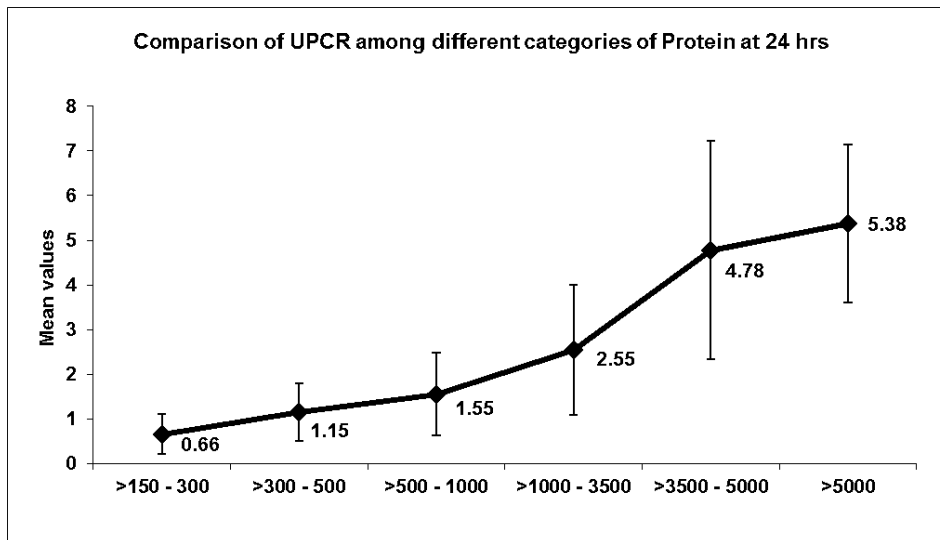


FIGURE I: The above analysis shows that the comparison of spot urine protein creatinine ratio among different categories of 24-hour proteinuria. It was found that as the 24-hour protein excretion increased the corresponding spot urine protein creatinine ratio also increased, with more accuracy at a lower range of protein excretion. ($P < 0.001$)

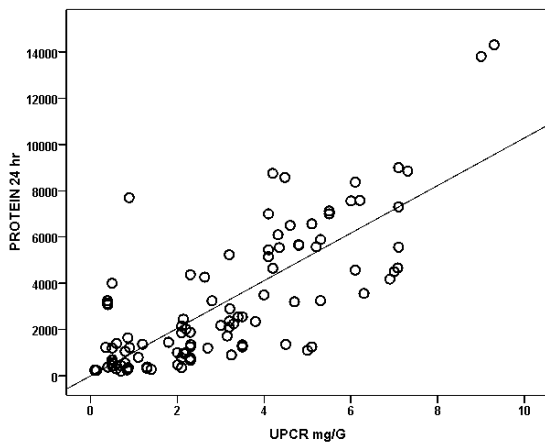


FIGURE II: Scatter plot diagram showing the positive relationship between 24-hour protein and spot protein creatinine ratio.

There was a positive relationship between UPCR and 24-hour urinary protein (Figure I & Figure II) with Pearson's correlation coefficient being 0.72 ($P < 0.001$). Interestingly, the correlation was much more accurate at the lower range of proteinuria.

DISCUSSION

Our study showed that there is a positive association between Urinary protein creatinine ratio and 24-hour urinary protein. (Pearson's correlation coefficient $r = 0.78$, $P < .001$). Also, this association was much stronger at a lower level of proteinuria.

Timed collection of the urine sample is a tedious, cumbersome procedure prone

to error. Highlighting this problem, samples of 12 patients (10%) had to be discarded because of improper collection. Mitchell et al. [12] in a study of the elderly patients, had to discard 20% of all the urine the samples because of the incomplete sample collection; Chitalia et al. [13] in their study had to discard 10% of the samples received for similar reasons. The NKF K/DOQI [14] guidelines suggest that spot urine samples should be used for diagnosis and follow up proteinuria in children and adults, it prefers a first-morning sample but accepts a random sample if a first-morning specimen is not available.

Several authors [15,16] have investigated the circadian variation in protein excretion and found that values can vary from 100% to 500%, which may be attributable to variation in water intake and excretion, the rate of diuresis, exercise, recumbency, and diet. Pathologic changes in blood pressure may further exacerbate the variation. An alternative approach to overcome this variation is to normalise the urinary excretion of the solute to the excretion of urinary creatinine. To support this proposal, several investigators have demonstrated a smaller variation in the protein creatinine ratio compared with the protein concentration alone in urine samples collected throughout the day. Thus,

Newman et al. [15] found that the mean intraindividual variation in the protein creatinine ratio was 38.6%, whereas that of the protein excretion was 96.5%. Koopman et al. [16] had made a similar observation.

Our study showed that correlation was much better at the lower level of proteinuria (Figure I). This is in concordance with other studies. Nuria Montero et al, [17] demonstrated that the protein creatinine ratio has a strong correlation with the 24-hour protein for values lower than 3500mg; however, they did not observe a correlation for proteinuria in the nephrotic range. Hence, in their group of study, as the degree of 24-hour protein increases, the degree of correlation decreases. In this respect, Antunes et al. [18] have also demonstrated that, the greater the proteinuria, the lesser the correlation and adjustment between the different methods. Using the Bland and Altman method, it was observed that as the 24-hour protein closer to the nephrotic range proteinuria, there is less concordance between the methods.

Our results agree with most of the authors; still there are some well-known conflicting results as reviewed extensively by BK Yadav et al. [19] This was a hospital-based cross-sectional study with small sample size and confined to the proteinuric patients only. It did not include the non-proteinuric patient. So, the finding of this study can not be extrapolated to use UPCR as a screening tool on OPD basis.

Our study confirms that UPCR can be used as a surrogate for 24-hour urinary protein in routine clinical practice for the diagnosis and also for the follow up of the patients who are on antiproteinuric medicines as the former had a stronger correlation at the lower level of proteinuria.

REFERENCES

1. Cravedi P, Remuzzi G. Pathophysiology of proteinuria and its value as an outcome measure in chronic kidney disease. *Br J Clin Pharmacol* 2013;76(4):516–23.
2. Hanly JG, O’Keeffe AG, Su L, et al. The frequency and outcome of lupus nephritis: results from an international inception

- cohort study. *Rheumatology* 2016;55(2): 252–62.
3. Liu G, Wang H, Le J, et al. Early-stage predictors for treatment responses in patients with active lupus nephritis. *Lupus* 2019;28(3):283–9.
4. Sarno L, Maruotti GM, Saccone G, et al. Pregnancy outcome in proteinuria-onset and hypertension-onset preeclampsia. *Hypertens Pregnancy* 2015;34(3):284–90.
5. Reich HN, Troyanov S, Scholey JW, et al. Remission of Proteinuria Improves Prognosis in IgA Nephropathy. *J Am Soc Nephrol* 2007;18(12):3177–83.
6. Kobayashi Y, Tateno S, Hiki Y, et al. IgA Nephropathy: Prognostic Significance of Proteinuria and Histological Alterations. *Nephron* 1983;34(3):146–53.
7. Methven S, Traynor JP, Hair MD, et al. Stratifying risk in chronic kidney disease: an observational study of UK guidelines for measuring total proteinuria and albuminuria. *QJM Int J Med* 2011;104(8):663–70.
8. Viswanathan G, Upadhyay A. Assessment of Proteinuria. *Adv Chronic Kidney Dis* 2011;18(4):243–8.
9. Levey AS, Inker LA. Assessment of Glomerular Filtration Rate in Health and Disease: A State of the Art Review. *Clin Pharmacol Ther* 2017;102(3):405–19.
10. Viswanathan V, Chamukuttan S, Kuniyil S, et al. Evaluation of a simple, random urine test for prospective analysis of proteinuria in Type 2 diabetes: a six year follow-up study. *Diabetes Res Clin Pract* 2000;49(2–3):143–7.
11. Patil P, Shah V, Shah B. Comparison of spot urine protein creatinine ratio with 24 hour urine protein for estimation of proteinuria. *J Assoc Physicians India* 2014; 62(5):406–10.
12. Mitchell SCM, Sheldon TA, Shaw AB. Quantification of Proteinuria: A Re-evaluation of the Protein/Creatinine Ratio for Elderly Subjects. *Age Ageing* 1993; 22(6):443–9.
13. Chitalia VC, Kothari J, Wells EJ, et al. Cost-benefit analysis and prediction of 24-hour proteinuria from the spot urine protein-creatinine ratio. *Clin Nephrol* 2001;55(6):436–47.
14. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis Off J*

- Natl Kidney Found 2002;39(2 Suppl 1):S1-266.
15. Newman DJ, Thakkar H, Medcalf EA, et al. Use of urine albumin measurement as a replacement for total protein. Clin Nephrol 1995;43(2):104–9.
 16. Koopman MG, Krediet RT, Koomen GCM, et al. Circadian Rhythm of Proteinuria: Consequences of the Use of Urinary Protein: Creatinine Ratios. Nephrol Dial Transplant 1989;4(1):9–14.
 17. Correlation between the protein/creatinine ratio in spot urine and 24-hour urine protein | Nefrología (English Edition) [Internet]. [cited 2019 Oct 19]; Available from: <http://www.revistanefrologia.com/en-estadisticas-X2013251412001579>
 18. Antunes VVH, Veronese FJV, Morales JV. Diagnostic accuracy of the protein/creatinine ratio in urine samples to estimate 24-h proteinuria in patients with primary glomerulopathies: a longitudinal study. Nephrol Dial Transplant 2008; 23(7):2242–6.
 19. Yadav BK, Adhikari S, Gyawali P, et al. Use of protein: creatinine ratio in a random spot urine sample for predicting significant proteinuria in diabetes mellitus. Nepal Med Coll J NMCJ 2010;12(2):100–5.

How to cite this article: Narula K, Verma SK, Ahmad S. Correlation of urinary protein creatinine ratio with 24-hour urinary protein in Indian patients. International Journal of Research and Review. 2020; 7(1): 506-510.
