

## Original Article

### Can Spot Urine Protein Creatinine Ratio be an alternative for the 24 Hour Urine Protein to estimate proteinuria in Chronic Kidney Disease? A comparative observational study

Raghavendra B L<sup>1</sup>, Varsha R Mokhasi<sup>2\*</sup>

1. Senior Resident, Department of Nephrology, JSS Medical College, JSS Academy of Higher Education and Research, Mysore.
2. Assistant Professor, Department of Community Medicine, Sri Devaraj Urs Medical college, Sri Devaraj Urs Academy of Higher Education and Research, Kolar.

#### Abstract

**Background:** The definition of CKD is its a non-reversible and the function of the kidneys reduces progressively. As the estimation of 24 hour urine protein levels is cumbersome, the current research aims to how valid is the use of the ration of Spot urine protein to creatinine in place of 24 hour method.

**Aims:** To compare UPCR with urine protein for 24 hours with respect to the stages 3 and 4 of CKD. To validate UPCR for estimating proteinuria in the stages 3 and 4 of CKD.

**Study setting and study design:** A comparative observational study among patients with the stages of 3 and 4 in CKD.

**Methods and Material:** A total of 90 patients in stages 3 and 4 of CKD were chosen for the study. All the 90 patients were subjected to UPCR and protein in urine for 24 hours to check validity of UPCR in comparison to gold standard.

**Statistical analysis :** The data analysis was done using SPSS. Significance tests: Chi-square and correlation.

**Results:** A positive correlation was observed among the subjects with CKD for both the urine protein for 24 hours and UPCR .In the stage 3, UPCR was found to have lower sensitivity and specificity. Whereas UPCR had good sensitivity in diagnosing the stage.

**Conclusions:** The present study showed UPCR to have good sensitivity and good specificity for CKD stage 4 than stage 3. Hence UPCR can be better indicator for CKD stage 4 than stage 3.

**Keywords:** CKD, 24 hour urine protein, Urine protein creatinine ratio

#### Introduction

The definition of CKD is that the kidney abnormality in terms of both structure and function persists for more than 90 days with implication for health. At

present the classification of CKD is given on the basis of a etiology, GFR and category of Albuminuria.<sup>1</sup>

The old as well as new cases of CKD in our country has found a increase over last 10 years with increase in expectancy of life and change in life-style, with a population of 6.3 to 7.2% found to have the stages 3 and 4 of CKD. This increase is accounted for the increase in the cases of diabetes and obesity.<sup>2</sup> Increased prevalence of CKD has translated into a 32.4% increase in years of life lost between 1990 and 2010.<sup>3</sup>

The contribution of proteinuria in CKD by several mechanism and measures for reduction of proteinuria is found to better the outcome, therefore

#### \*Corresponding Author

**Dr. Varsha R Mokhasi**

Assistant Professor, Department of Community Medicine, Sri Devaraj Urs Medical College, Sri Devaraj Urs Academy of Higher Education and Research, Kolar-563101, Karnataka, India.

Mobile No : 9663696854

E-mail : varshambbs47@gmail.com

Conflict of Interest: None

Financial Aid: Nil

a correct proteinuria assessment is necessary in managing CKD.<sup>4</sup>

In terms of actual care of patients, collection of 24 hours urine is a difficult task and it has also been found to have a collection error n in 12-15% samples. The excretion of Creatinine both in patients with CKD and normal people is not explored and thereby in both cases, the use of ratio of urine protein and ratio in measuring proteinuria is not validated.<sup>5</sup>

## Material and Methods

### Study design

This is a comparative observational study conducted in the government tertiary care center. A sample of 90 patients' urine with the stage 3 & 4 of CKD which had both males and females was collected. All the samples tested for 24 hour protein in urine estimation and also the ratio of urine protein and creatinine.

### Method of collection

The sample calculation was done by selecting the proportion of patients with the stage 3 of CKD as 6.3% as found by an observational study conducted in Karnataka with 5% absolute error and 95% confidence interval.<sup>6</sup> The study was carried out between January 2015-June 2016(18 months).

### Inclusion Criteria

All patients in the ages 18-70 years with the stages 3 and 4 of CKD, who gave an informed consent.

#### CKD criteria (any one present for more than 90 days)

The kidney destruction markers (more or equal to 1)

- Albumin in urine (more than 30 milli grams per day)
- Abnormality in sediments of urine
- Tubular diseases causing imbalance in electrolytes
- Histology showing any abnormalities
- Defect in structure found in imaging
- **Decrease in GFR:** GFR 15-65 mili litreper minute)

Patients with Fever, Acute failure of kidneys, Urinary tract infection ,Haematuria (gross) ,Pregnant women were excluded Criteria

### Statistical Analysis

The entry of data was with Microsoft excel. The coding of variables which are qualitative and the analysis of data was done by using the SPSS software.

The data being collected was being summarized and was presented in form of frequency, mean, proportion and SD, which in turn depends if the variables are quantitative or qualitative.

The significance tests and for association were Chi-square test and correlation. If the p value was more than 0.051, it was found to be significant statistically. The plot of Receiver operator characteristic curve was used to find the pattern of sensitivity and specificity.

### Ethical consideration

The study was approved by the board for ethical review at Government Medical College at Mysore.

The consent was taken from the patients before the start of study. The patient identity was kept anonymous at all the levels of analysis of data.

## Results

### Patient Characteristics

The table provided below gives an overview regarding characteristics of the patients. Majority of patients belonged to >60 years age group. The distribution as per gender showed that majority of subjects were males (77.8%) and 22.2% were women. In the present study 34.4% had a CKD Stage of 3 and 59% of them Stage 4 CKD. (Table 1)

Table 1: Patient Characteristics.

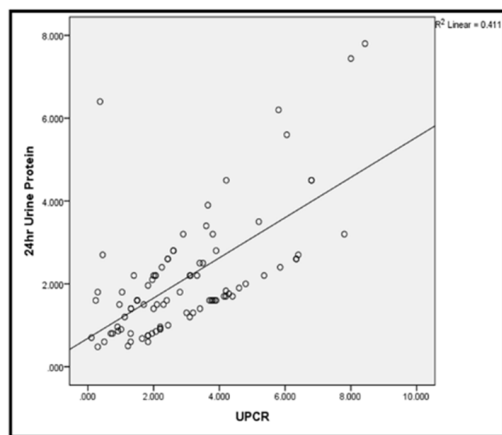
Patient Characteristic		Count	%
Age	<40 years	13	14.4%
	41 to 50 years	20	22.2%
	51 to 60 years	26	28.9%
	>60 years	31	34.4%
	Total	90	100.0%
Gender	Male	70	77.8%
	Female	20	22.2%
	Total	90	100.0%
CKD Stage	Stage 3	31	34.4%
	Stage 4	59	65.6%
	Total	90	100.0%

### Urine Protein for 24 hours and ratio of Urine Protein and Creatinine correlation

There was a significant Correlation at a level of 0.01 with Pearsons correlation value of 0.641 which (Table 2). The correlation was found to be positive and significant between the Urine protein for 24 hours and UPCR among patients. I.e. with increase in Urine protein for 24 hrs there was raise in ratio of Urine Protein Creatinine and Vice versa is depicted by the scatter plot. (Figure 1)

**Figure 1: Scatter Plot showing Positive correlation between 24 hour Urine Protein and UPCR.**

Figure 1: Scatter Plot showing Positive correlation between 24 hour Urine Protein and UPCR



### UPCR: Sensitivity and also Specificity

Both sensitivity of UPCR and specificity was shown to be poor to diagnose stage 3 CKD at different percentile levels of UPCR as given by Table 3. It is supported with Receiver Operator Characteristic (ROC) curve which shows the area below the curve being much lesser than 1(0.21). (Figure 2)

Where as the UPCR had good sensitivity in diagnosis of CKD Stage 4 (Table 4). Area below the curve was close to 1 (Figure 3). Hence UPCR can be better indicator for CKD stage 4 than stage 3.

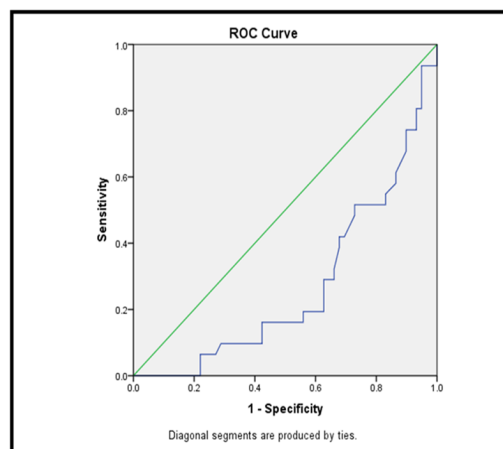
**Table 2: Correlation between 24hr Urine Protein and Urine Protein Creatinine ratio.**

Correlations			
		24hr Urine Protein	UPCR
24hr Urine Protein	Person Correlation	1	0.641**
	Sig. (2-tailed)		<0.001*
	N	90	90

\*\*Correlation is significant at the 0.01 level (2-tailed).

**Figure 2: ROC curve showing Area under curve for UPCR in diagnosis of CKD stage 3.**

Figure 2: ROC curve showing Area under curve for UPCR in diagnosis of CKD stage 3



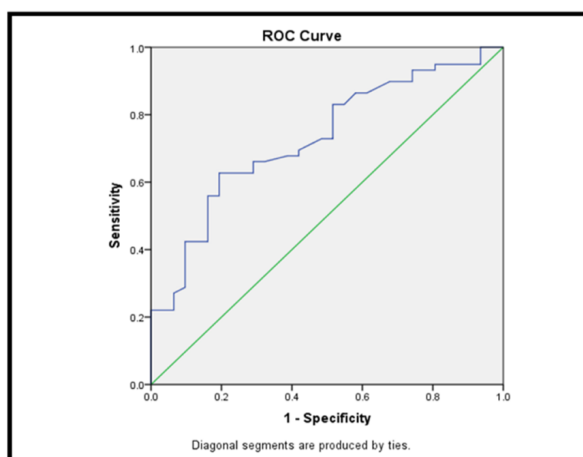
**Table 3: Urine Protein Creatinine Ratio in diagnosis of CKD stage 3**

Area Under the Curve				
Test Result Variable(S): UPCR				
Area	SE	P value	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.271	0.054	<0.001*	0.165	0.377

UPCR value	Sensitivity	Specificity
1.5	0.58	0.13
2.43	0.22	0.37
3.9	0.097	0.66

**Figure 3: ROC Curve showing Area under curve for UPCR in CKD stage 4**

Figure 3: ROC Curve showing Area under curve for UPCR in CKD stage 4



**Table 4: Urine Protein Creatinine Ratio in diagnosis of CKD stage 4**

Area Under the Curve				
Test Result Variable(S): UPCR				
Area	SE	P value	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.729	0.054	<0.001*	0.623	0.835

UPCR value	Sensitivity	Specificity
1.50	0.86	0.42
2.43	0.62	0.77
3.90	0.33	0.90

## Discussion

Amongst the CKD patients, urinary protein measured for a day is used to diagnose and to check of proteinuria periodically. But the ratio of urine protein and creatinine is very easy and less costly method to assess how severe is the kidney disease and its prognosis. The ratio of urine protein creatinine is very helpful in case of difficulty in collecting urine for a day and in case of people requiring repeated assessment. National Kidney Foundation (USA)<sup>7</sup> as well as Australian society for Hypertension study<sup>8</sup> have recommended ratio of urine protein creatinine instead of the estimate of urine protein tested for a day.

The present study included stage 3 & 4 of CKD patients to find out how reliable is the ratio of urine protein and creatinine to analyse proteinuria by correlating and the extent of association by comparison of urine protein for a day.

This study expressed that the coefficient for correlation (value of r) between ratio of urine protein and creatinine and urine protein for a day when repeated on a scale of log was 0.644 (P<0.001). Therefore, it showed that there is correlation which was positive in relation to both between estimate of urine protein for a day with a increase of in ratio of urine protein creatinine.

A study by Nayak R et al showed that the reliability of ratio of urine protein creatinine used in determining proteinuria in the stage 3 & 4 of CKD, the ratio of urine protein and creatinine was found to have accurate similarity with the estimate of urine protein for a day quite, the co-efficient of correlation, with value of r being 0.84 in the scale of log with a significant value of p. It also found that there was a good agreement between the above mentioned proteinuria assessment methods.<sup>9</sup>

A similar finding was shown by Chitalia and the co-authors in a forward looking cross-section

study. This study included a variety of glomerular disease patients (total of 170 patients) and was conducted to observe how accurate is the ratio of urine protein and creatinine with respect to the value of urine protein for a day. It was shown to have very significant positive co-relation with r value close to one among the two parameters. Blom Altmann method was used to evaluate agreement level. All the findings came with the significant agreement level<sup>10</sup>

In a study by Antunes which proposed to find the accurate diagnostic capacity of the ratio of urine protein and creatinine to find the proteinuria in a day in Brazil. The observation was that the correlation was positive and significant between ratio of urine protein creatinine and Urine protein being estimated for an entire day with p value less than 0.0001 and coefficient of K being 0.87. The agreement level was shown in terms of coefficient of kappa.<sup>11</sup>

The study found that the sensitivity was poor for the ratio of urine protein and creatinine and so was the specificity to diagnose stage 3 of CKD at percentile of different level but had a sensitivity of 86% which was quite good for diagnosing of Stage 4 CKD. In this particular study, level of urine protein estimated in a day had sensitivity along with specificity at poor levels in diagnosis of stage 3 CKD when compared to Stage 4 CKD with a sensitivity value of 84%. The area under curve was nearly equal to one in the ROC curve in case of both ratio of urine protein and creatinine and urine protein estimated in a day, this indicates that ratio of urine protein and creatinine will be better in case of diagnosing 4<sup>th</sup> stage CKD than the stage 3. This finding was similar to that found by Nayak, here the under curve area in ROC curve was also near to one, thus concluding that this is a preferable test in detecting protein in urine of value more than 150 mili gram per day.<sup>9</sup>

A study by Patil P to evaluate as well as for standardization of the method of the ratio of urine protein and creatinine to find proteinuria. This was a study which included 241 patients in Bombay. The finding was that ratio of urine protein creatinine value (0.1171) predicted the total urine protein with reliability almost equal to more than 150 mili gram per day, there was 100% sensitivity and specificity of 98.1 % as given by the ROC curve.<sup>12</sup>

Another finding which was of importance in the study was that the ratio of urine protein creatinine showed a predictive value of higher value in case of decline rate of GFR with p value of 0.01 in the stages 3 & 4 CKD. The negative correlation was significant with r value of minus 0.317 between the ratio of urine protein & creatinine and GFR. It was seen that the increase in urine protein for a day had association with the lowering of GFR and vice versa. The negative correlation level of ratio of urine protein creatinine with the GFR was found to be significant in compari-

son with the estimate of urine protein for a day ( $r=0.290$ ). Significant positive correlation ( $r=0.289$ ) was seen with respect to both between ratio of urine protein creatinine, with increase in UPCR there was increase in Creatinine and vice versa.

In another observational study, in Italy, including 177 patients with CKD, conducted by Ruggerenti P, ratio of urine protein and creatinine showed to be of a high predictive value with respect to the decline rate of GFR with a significant value of  $p$  and ESRD, the  $p$  values were 0.002 and 0.04. The multivariate analysis found the ratio of urine protein creatinine has significant predictive value in case of a faster decrease in GFR in comparison with the estimate of urine protein in 24 hours.<sup>1</sup>

## Conclusion

The Spot UP/C ratio reliably predicted proteinuria in present study among CKD stage 3 and 4 patients with a significant positive correlation with the 24 hour urine protein value. However, the UPCR had poor sensitivity and specificity in diagnosis of CKD stage 3 but a higher sensitivity in case of stage 4. The UPCR was also found to have a higher predictive value for rate of decline of the glomerular filtration rate than the 24 hour urine protein. Therefore, the UPCR represents a simple and inexpensive procedure in establishing severity of renal disease and prognosis.

## References

1. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int* 2013; 3:1-150.
2. Agarwal SK, Srivastava RK. Chronic kidney disease in India: challenges and solutions. *Nephron clinical practice* 2009; 111(3):c197-203.
3. Rajapurkar MM, John GT, Kirpalani AL, Abraham G, Agarwal SK, Almeida AF, Gang S, Gupta A, Modi G, Pahari D, Pisharody R. What do we know about chronic kidney disease in India: first report of the Indian CKD registry. *BMC nephrology* 2012 Dec; 13(1):10.
4. Kutlugün AA, Arıcı M, Yıldırım T, Turgut D, Yılmaz R, Altındal M, Altun B, Erdem Y, Yasavul Ü, Turgan C. Daily sodium intake in chronic kidney disease patients during nephrology clinic follow-up: an observational study with 24-hour urine sodium measurement. *Nephron Clinical Practice* 2011; 118(4): 361-6.
5. Methven S, MacGregor MS, Traynor JP, O'Reilly DS, Deighan CJ. Assessing proteinuria in chronic kidney disease: protein-creatinine ratio versus albumin-creatinine ratio. *Nephrology Dialysis Transplantation* 2010; 25(9):2991-6.
6. Varma PP. Prevalence of chronic kidney disease in India-Where are we heading?. *Indian journal of nephrology* 2015 ;25(3):133
7. Plantinga LC, Fink NE, Harrington-Levey R. Association of social support with outcomes in incident dialysis patients. *Clin J Am Soc Nephrol* 2010; 5(8):1480-8.
8. Vassalotti JA, Stevens LA, Levey AS. Testing for chronic kidney disease: a position statement from the National Kidney Foundation. *Am J Kidney Dis* 2007; 50:169-80.
9. Brown MA, Hague WM, Higgins J, Lowe S, McCowan L, Oats J. The detection, investigation and management of hypertension in pregnancy: executive summary. *Aust N Z J Obstet Gynaecol* 2000; 40:133-8.
10. Nayak R, Annigeri RA, Vadmalai V, Seshadri R, Balasubramanian S, Rao BS, et al. Accuracy of spot urine protein creatinine ratio in measuring proteinuria in chronic kidney disease stage 3 and 4. *Indian J Nephrol* 2013;23 (6):428-33.
11. Price CP, Newall RG, Boyd JC. Use of protein:creatinine ratio measurements on random urine samples for prediction of significant proteinuria: a systematic review. *Clin Chem* 2005; 51 (9):1577-86.
12. Chitalia VC, Kothari J, Wells EJ, Livesey JH, Robson RA, Searle M, Lynn KL. Cost-benefit analysis and prediction of 24-hour proteinuria from the spot urine protein-creatinine ratio. *Clin Nephrol* 2001; 55:436-47.
13. Ginsberg JM, Chang BS, Matarese RA. Use of single voided urine samples to estimate quantitative proteinuria. *N Engl J Med* 1983; 309(25):1543-6.
14. Abbate M, Zoja C, Remuzzi G. How does proteinuria cause progressive renal damage? *J Am Soc Nephrol* 2006;17(11):2974-84.
15. Go AS, Chertow GM, Fan D. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med* 2004; 351(13):1296-305.
16. Crowe E, Halpin D, Stevens P. Guideline Development Group: Guidelines— Early identification and management of chronic kidney disease: summary of NICE guidance. *BMJ* 2008; 337(7673):a1530.
17. Abboud H, Henrich WL. Stage IV chronic kidney disease. *N Engl J Med* 2010; 362(1):56-65.
18. Curtis BM, Barrett BJ, Djurdjev O. Evaluation and treatment of CKD patients before and at their first nephrologist encounter in Canada. *Am J Kidney Dis* 2007;50(5):733-42.
19. Hemmelgarn BR, Manns BJ, Zhang J. Association between multidisciplinary care and survival for elderly patients with chronic kidney disease. *J Am Soc Nephrol* 2007; 18(3):993-9.
20. 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; 62:406-10.