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Correlation of spot urinary protein creatinine ratio with 24-hours urinary protein in different stages of chronic kidney disease - A Single center study

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Abstract

Aim and objectives: To correlate spot urine protein creatinine ratio (UPCR) with 24 hours urinary protein in patients with chronic kidney disease (CKD) at tertiary care centre.

Material and Methods: This was a prospective observational study included 155 adult CKD patients coming to outpatient nephrology department at Institute of Kidney Disease and Research Center, Institute of Transplantation sciences (IKDRC-ITS) to establish correlation between 24 hr urinary protein and spot UPCR in different stages of CKD as per Kidney Disease Improving Global Outcomes (KDIGO) guideline.

Results: We included 155 patients as per inclusion and exclusion criteria with mean age of 39 ± 13 years with 116:39 (M: F) ratio. On analysis of all patients, mean 24 hours proteinuria and spot UPCR were 2.99 ± 4.1 gm and 4.37+-6.3 respectively. We observed no statistically significant difference between both tests in CKD stage 1

to 4 (p value >0.05), whereas significant difference was noted in CKD stage-5(p value<0.05).

Conclusion: To conclude, although spot UPCR level showed good linear correlation with gold standard 24-hours urinary protein in patient with early stage of CKD, it was not correlating well in CKD stage 3, stage 4 and stage 5 probably. So, the spot UPCR can't replace gold standard 24 hours proteinuria in CKD patient.

Keywords: proteinuria in CKD, 24 hours urine proteinuria, urine protein: creatinine ratio

Introduction

The prevalence of chronic kidney disease (CKD) is increasing worldwide and timely diagnosis is crucial to preserve renal function [(1)]. Urine analysis for proteinuria is an essential element for diagnosis, assessment of disease severity and monitoring of treatment response in many chronic renal diseases. The presence of proteins in the urine together with the estimation of glomerular filtration rate (eGFR) constitutes a sign of kidney damage and, it is useful for the evaluation of chronic kidney disease (CKD) staging [(2)]. Proteinuria also identifies the patients with high risk of progressive kidney damage [(3,4)]. Estimation of 24 hours urine protein has been considered as gold standard to determine excretion of urine protein. However, this method of collecting 24 hours urine sample is time consuming and cumbersome to the patients. It can be affected by many factors including over or under collection of urine, proper storage, duration of collection and also inconvenient for repeated monitoring. Therefore, many clinicians are prescribing spot urine protein creatinine ratio (UPCR) for estimation of proteinuria in patients with renal diseases, [(5,6,7)]. The spot UPCR test is based on the concept of steady ratio of creatinine and protein excretion in urine and believed to be equivalent of 24 hours urinary protein excretion [(8)]. There are many studies which compared the 24 hours proteinuria with spot UPCR and showed variable outcome for their correlation. Many studies also concluded spot UPCR could be affected by many factors like type glomerular disease, degree of proteinuria, renal function, diurnal variation etc.

So, in this study we have evaluated correlation of 24 hours urinary protein with spot UPCR in different groups based on CKD staging as per kidney disease initiative global outcome (KDIGO) guideline [(9)].

Material and Methods

This was a prospective observational single center study to evaluate correlation between 24 hours urinary protein with spot UPCR in chronic kidney disease patients who visited at nephrology OPD at our institute between 1st February'22 to 16th March'23.

Patients were included and excluded from the study as per inclusion and exclusion criteria.

Inclusion criteria

- Chronic kidney disease patients of any stage as per KDIGO guideline with age above 18 years and any gender[9]

Exclusion criteria

- Patients <18 years of age
- Pregnant or lactational women with CKD
- Presence of mucus and pus cells (>6/ hpf) in recent urine routine and microscopy report
- Patient who fails to give spot urinary samples

The study population was divided in 5 groups based on CKD staging as per KDIGO guideline [(9)]. The eGFR was calculated with CKD-EPI formula for eGFR based CKD staging. Initially, total 180 patients were selected for the study, out of which 24 patients were dropped out due to violation of any of the inclusion criteria. Finally, total 155 patients were recruited in the study population and were divided in five groups as per shown in Fig.1.

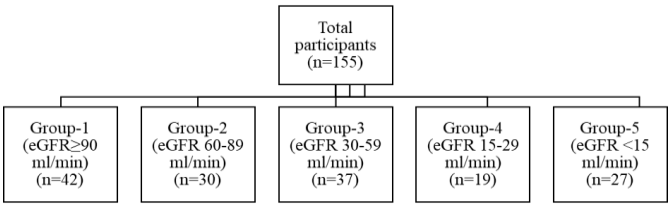

Fig. 1: Division of study population in 5 groups based on e-GFR

We compared 24 hours urinary protein with spot UPCR in all five groups.

Collection urine sample

All participants were provided 24 hours urinary sample collection container with preservative and instructed to collect urine sample as per standard protocol explained to them. The patients were also asked to provide spot urinary sample when they came to submit 24 hours urinary sample container.

Analysis of samples

24 hours urinary samples were analyzed for volume and protein concentration, whereas all spot urinary samples were analyzed for protein and creatinine concentration. The spot UPCR was calculated for all spot samples and were compared with respective 24 hours urinary protein concentration. Urinary protein concentration was measured by pyrogallol red colorimetric method on fully automated analyzer Exl dimension (Siemens, Germany). The creatinine concentration in spot samples were analyzed by Isotropic dilutional mass spectrometry (IDMS) traceable modified Jaffe's method on fully automated biochemistry analyzer AU-480 (Beckman Coulter, USA). This study was approved by institutional ethics committee.

Statistical analysis

All values in all groups were expressed as mean ± SD. Comparison of 24 hours urinary protein with spot UPCR were made with Mann whitney test and correlations were calculated with Pearson correlation coefficient and r value by using GraphPad Instant version 3.03 statistical software. A p value < 0.05 was considered as statistically significant.

Results

In our study, total 155 patients were recruited with mean age of 39 ± 12.8 years with 116 (75%) male and 39 (25%) female patients.

In group 1, mean 24 hours urinary protein level was 2.32 ± 2.75 gm whereas mean spot UPCR was 3.19 ± 4.2 So, when p value was calculated between two tests, no statistically significant difference was noted between them (p=0.3639). On comparison of both samples in group 2, we found no statistically significant difference with mean of 3.11 ± 5.82 gm and 4.27 ± 8.54 in 24 hours and spot UPCR sample respectively (p=0.2973). The same observations were noted in group-3 and group-4 with no statically significant difference between 24 hours urinary protein and spot UPCR (Group 3: p value=0.6773, Group 4: p value=0.3972). The mean of 24 hours proteinuria and spot UPCR were 3.35 ± 4.94 gm and 3.87 ± 5.09 respectively in group 3, and 2.56 ± 2.75 gm and 4.09 ± 5.78 respectively in group 4. On comparison in group 5, patients having e-GFR less than <15 ml/min, found to be having statistically significant difference between 24 hours protein level and spot UPCR sample (p<0.05) with mean of 3.67 ± 3.03 gm and 7.18 ± 7.39 respectively (Table-1). So, there was no statistically significant difference between two tests in CKD stage 1 to 4, whereas CKD stage-5 showed significant difference between two.

Table 1: Comparison of 24 hours urinary protein with spot UPCR in all groups

CKD stage (group)	No. of Participant (n=155)	24 hours proteinuria (gm/day)			Spot UPCR			p value
		Mean ± SD	Min	Max	Mean ± SD	Min	Max	
Group-1 (CKD Stage-1)	42	2.32 ± 2.75	0.02	9.3	3.19 ± 4.2	0.13	18.2	0.3639
Group-2 (CKD Stage-2)	30	3.11 ± 5.82	0.07	26.5	4.27 ± 8.54	0.04	45.5	0.2973
Group-3 (CKD Stage-3)	37	3.35 ± 4.94	0.13	26.0	3.87 ± 5.09	0.18	22.2	0.6773
Group-4 (CKD Stage-4)	19	2.56 ± 2.75	0.24	10.4	4.09 ± 5.78	0.3	25.2	0.3972
Group-5 (CKD Stage-5)	27	3.67 ± 3.03	0.51	11.8	7.18 ± 7.39	0.7	26.3	0.0162 (<0.05)

The correlation coefficient between two methods showed positive correlation with coefficient (r) value of 0.67 in the overall study population with variable regression correlation in individual staging of CKD (Fig-2). The correlation of spot UPCR and 24-hours urinary protein were very high in CKD stage-1 (r=0.87) and stage-2 (r= 0.85) in comparison with CKD stage-3 (r=0.64), stage-4 (r=0.46) and stage-5 (r=0.63).

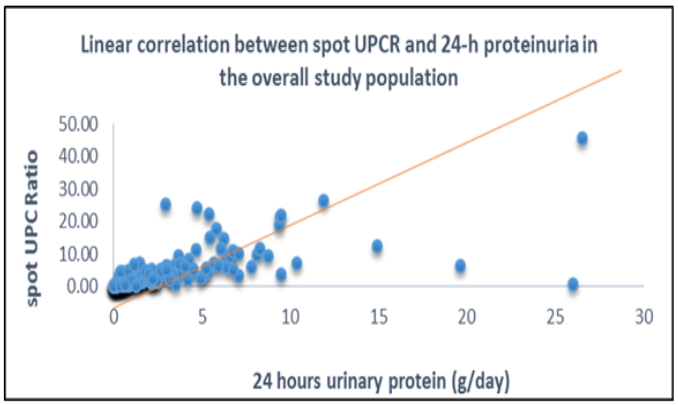

Fig 2: Linear correlation between spot UPCR and 24-h proteinuria in the overall study population

Discussion

Quantification of proteinuria is vital for monitoring disease activity and response to therapies in patients with glomerular disease. The 24 hours urinary protein measurement is considered the gold standard method for urinary protein excretion. However, 24 hours urinary collection is tedious and cumbersome procedure which is prone to many pre-analytic errors like volume, storage, duration etc. It is also inconvenient for repeated monitoring in follow-up cases. Nowadays, many clinicians are prescribing protein excretion rate in the form of spot UPCR, considering better patient compliance for sample collection but correlation of spot UPCR with 24 hours urinary protein is still challenging to quantify protein excretion rate especially in altered renal function.

Our study showed that spot PCR is correlating with 24 hours proteinuria in CKD stage 1 to 4, but there was significant difference between two of them in stage 5 of CKD. Moreover, we found strong positive correlation

with 24 hours proteinuria and spot UPCR in overall study population (r=0.67). The correlation between two tests were high in CKD stage-1 (r=0.87) and stage-2 (r= 0.85) in comparison of stage-3 (r=0.64), stage-4 (r=0.46), stage-5 (r=0.63). These findings suggest that spot UPCR was not correlating well with 24 hours urinary protein in CKD stage 3,4 and 5, possibly due to effect of decreasing eGFR with advancing kidney disease. These findings were supported by Nayak et al, who studied correlation of these two tests in 100 patients of CKD stage 3 and stage 4, found good correlation between 24-hour proteinuria and spot UPCR in CKD stage 3 and 4 (r = 0.86). They noticed correlation was better in CKD stage-3 than CKD stage-4 [10]. The possible cause of this variation in different staging is decrease in eGFR with advancement of CKD. Krishnamurthy H et al also studied the correlation of both tests in 120 patients of CKD and their observation is almost matching with our findings. They observed spot UPCR is correlating with 24 hours proteinuria in assessment kidney function in different stages of CKD, specially stage 3 and 4 CKD **[11]**. These findings are also similar with our study. In addition of these, they observed eGFR is more negatively correlated with spot UPCR then 24 hours urinary protein level.

In contrast to our study, Davut Akin et al also investigated the relationship between spot UPCR and 24-h protein excretion in 644 adult patients with different clinical diagnosis. They concluded that spot UPCR cannot replace 24-h proteinuria due to low accuracy of random spot UPCR level possibly due the different timing of random urine collection, the amount of proteinuria and kidney function, type of kidney disease and the handling of urine samples [12]. Our study is also supported by Boon Wee Teo et al., who studied the correlation of these two tests in 232 CKD patients and concluded both test methods are interchangeable for assessment of protein excretion rate, but they have not classified study population based on different staging of CKD [13]. In another prospective study carried out by Antunes VV et al on 41 adult patients with primary glomerulopathy, showed diagnostic accuracy of spot UPCR to 24 hours proteinuria, and also established significant positive correlation between 24 hours proteinuria and spot UPCR ($p<0.05$, correlation coefficient-0.98) [14]. The similar findings were observed by Patil P et al showing UPCR as reliable, simple marker in routine practice [15].

Conclusion

In summary, though spot UPCR results showed good linear correlation with gold standard 24-hours urinary protein in patient with early stage of CKD, it was not correlating well in CKD stage 3, stage 4 and stage 5 probably due to effect of decreasing GFR with advancing disease. The spot UPCR can't replace gold standard 24 hours proteinuria in CKD patient despite of tedious, cumbersome and susceptible to errors 24 hours urinary collection. The additional studies with larger number of populations to evaluate correlation of 24 hours urinary protein and spot UPCR with clinical outcome are still warranted.

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