THE SPOT URINE PROTEIN CREATININE RATIO- HAS IT GOT REAL SIGNIFICANCE IN STAGING OF CHRONIC KIDNEY DISEASES?

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ABSTRACT

BACKGROUND

Proteinuria contributes to progression of chronic kidney disease by several mechanisms. Hence accurate assessment of proteinuria is an essential part of management of chronic kidney disease. In clinical practice, 24 hr urine collection is cumbersome and also error in the collection is seen in 10-20% of samples. So Spot urine protein creatinine ratio could be most suitable and less time-consuming method without compromising quality of assessment of proteinuria.

MATERIALS AND METHODS

Urine sample of 120 subjects, age between 18 to 70 years with chronic kidney disease was collected. The total 24 hours protein by turbidometric method and the spot urine protein creatinine ratio was taken. The urine creatinine was measured by Jaffe's method.

RESULTS

In this study, UPCR of stage 3 CKD is 1.9 ± 0.56 gm/ gm of creatinine, stage 4 CKD is of 3.5 ± 0.88 gm/gm of creatinine and that of stage 5 CKD is of 4.1 ± 0.78 gm/gm of creatinine.

The 24 hours urine value of CKD stage 1 is 1.1 ± 0.4 gm/ 24 hours, that of stage 2 is 1.6 ± 0.67 gm/24 hours, that of stage 3 is 1.8 ± 0.77 gm/24 hours, that of stage 4 is 3.6 ± 0.58 gm/24 hours and that of stage 5 is 3.9 ± 0.85 gm/ 24 hours. There is significant correlation found between the above values [p value<0.05].

CONCLUSION

The UPCR is non-inferior to 24 hours protein estimation in assessing the function of kidney in CKD cases. So UPCR is a simple and cost-effective test in establishing the severity of Chronic kidney diseases and to predict the prognosis.

KEYWORDS

CKD, GFR, UPCR.

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BACKGROUND

The Chronic kidney disease is defined as abnormalities of kidney structure or function, present for > 3 months. The chronic kidney disease is classified based on Causes, Glomerular filtration rate and Albuminuria. The prevalence rate of CKD stage 1 and 2 is 6%, for stage 3 and 4 is 4.5%.[1,2,3] The Proteinuria contributes to progression of chronic kidney disease by several Mechanisms. Hence accurate assessment of proteinuria is an essential part of management of chronic kidney disease. In clinical practice 24 hr urine collection is cumbersome and also error in the collection are seen in 10-20% of samples. So that Spot urine protein creatinine ratio could be most suitable and less time-consuming method without compromising quality of assessment of the proteinuria.[4,5,6]

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Aims and Objectives

To compare the significance of spot urine protein creatinine ratio with 24 hours urine protein level in staging of chronic kidney diseases.

MATERIAL AND METHODS

Source of Data

Urine sample of 120 subjects with chronic kidney disease including both male and female were used to get the required information using primary source of information technique with observation method.

Method of Collection

- Sample size: 120
- Study design: observational and comparative study
- Duration of study

Total study time- 6 months.

Inclusion Criteria

The patients aged between 18-70 years with chronic kidney disease, who are able to give valid informed/written consent.

Criteria for CKD (either of the following are present for >3 months) **Markers of kidney damage (one or more)**

- Albuminuria (AER >30 mg/24 hours; ACR >30 mg/g [>3 mg/mmol])
- Urine sediment abnormalities
- Electrolyte and other abnormalities due to tubular disorders
- Abnormalities detected by histology
- Structural abnormalities detected by imaging

Decreased GFR- GFR 60-15 ml/min/1.73 m2 (GFR categories G3–G4)

Exclusion Criteria

- Febrile illness
- Acute renal failure
- Urinary infection
- Gross haematuria
- Pregnancy

Total protein in urine was measured by chemical, turbidimetric, and dye binding (colorimetric) methods. The spot UPCR was obtained by dividing the urine protein concentrations by the urine creatinine concentration and expressing the result as mg/g. Both enzymatic and Jaffe assays are used for the measurement of creatinine in urine For men the normal urinary creatinine concentration range was found to be 18.5 to 25.0 mg per kg of body weight per day, and for women of the same age, 16.5 to 22.4 mg/kg/day.[7]

Statistical Analysis

Data was entered into Microsoft excel. The qualitative variables were coded, and analysis was done using R statistics software {Statistical package for the social sciences (SPSS) for windows version 22}.

The collected data was summarized and presented as frequencies, proportion, mean and standard deviation, depending on the quantitative or qualitative variables.

Chi-square test and correlation tests were used to test significance and associations. Analysis was performed using p value less than 0.05 was considered as statistically significant. Receiver operator characteristic curve was plotted to know the sensitivity and specificity pattern.

Ethical Consideration

This study was done after obtaining ethical clearance by the Institutional Ethics Committee, Mysore Medical College and Research Institute, Mysuru- 570021, with the no. EC REG: ECR/134/Inst/KA/2013. Anonymity of the respondents at all stages of data analysis was maintained. Informed consent in written form was taken before conducting the study.

The study received approval by the research review board and the ethical review board of Mysore Medical College and Research Institute. Verbal informed consent was obtained from the participants before proceeding the study. Anonymity of the respondents at all stages of data analysis was maintained. Informed consent in written from was also taken before conducting the study.

RESULTS

In this study 120 cases were included, in that 52(43.33%) were male and 68(56.66%) were female cases. The age distribution was between 18 to 70 years, in that 33(27.5%) were between 55 to 65 years, 50(41.66%) were in the age group of above 65 years. [Table 1]

Age Distribution (years)	Number of CKD Cases (%)	Gender	No. of CKD cases (%)
<45	16 (13.33)	Male	52(43.33)
45 to 55	21 (17.5)		
55 to 65	33 (27.5)	Female	68(56.66)
>65	50 (41.66)		

Table 1. Age and Gender Distribution of Cases

The CKD cases were classified in to five stages based on GFR. The normal GFR is between 80 to 120 ml/min/1.73 m^2 of body surface area. The CKD stage 3 cases were 31(25.83%), stage 4 were 56(46.66%) and stage 5 cases were 10(8.33%). [Table 2].

CKD Stage	No. of Cases (%)
Stage 1	8 (6.66)
Stage 2	15 (12.5)
Stage 3	31 (25.83)
Stage 4	56 (46.66)
Stage 5	10 (8.33)

Table 2. CKD Stage Among Subjects in the Study

The spot urine protein creatinine ratio is an important test done to know, whether there is a glomerular injury or tubular injury of kidney and also done to know the extent of damage to Kidney. In this study UPCR of stage 3 CKD IS 1.9 ± 0.56 gm/gm of creatinine, stage 4 CKD is of 3.5 ± 0.88 gm/gm of creatinine and that of stage 5 CKD is of 4.1 ± 0.78 gm/gm of creatinine [Table. 3]

Stage of CKD	UPCR (gm/gm of Creatinine) mean ± Standard Deviation
Stage 1	1.2 ± 0.6
Stage 2	1.5 ± 0.5
Stage 3	1.9 ± 0.56
Stage 4	3.5 ± 0.88
Stage 5	4.1 ± 0.78

Table 3. Urine Spot Protein to Creatinine Ratio (UPCR)

Stage of CKD	UPCR (gm/Gm) mean ± SD	24 hours Urine Protein (gm/24 hours) Mean±SD	P value <0.05
Stage 1	1.2 ± 0.6	1.1 ± 0.4	
Stage 2	1.5 ± 0.5	1.6 ± 0.67	
Stage 3	1.9 ± 0.56	1.8 ± 0.77	
Stage 4	3.5 ± 0.88	3.6 ± 0.58	
Stage 5	4.1 ± 0.78	3.9 ± 0.85	

Table 4. Correlation of UPCR to 24 hours Urinary Protein

The 24 hours urine report of CKD stage 1 is 1.1 ± 0.4 gm/24 hours, that of stage 2 is 1.6 ± 0.67 gm/ 24 hours, that of stage 3 is 1.8 ± 0.77 gm/ 24 hours, that of stage 4 is 3.6 ± 0.58 gm/ 24 hours and that of stage 5 is 3.9±0.85 gm/24 hours. The UPCR values were correlated with 24 hours urinary protein values, which were almost similar and were statistically significant with the p value of< 0.05. [Table. 4]

DISCUSSION

In patients with chronic kidney disease, 24-hour urinary protein estimation is used for diagnosis and follow up of proteinuria. However, the spot urine protein creatinine ratio (UP/C) is a inexpensive and simple test used to determine the severity of renal disease and its prognosis. It is especially useful in cases where it is difficult to collect 24 hours urine for protein estimation and for those who require repeated follow up. The Australian society for study of Hypertension[8] and the National Kidney Foundation (USA)[9] have recommended urinary spot Urine protein creatinine ratio as an alternative to 24-hour urine collection for urine protein estimation. Some Asian studies have also said that spot UP/C ratio to be more reliable predictor in decline in glomerular filtration rate compared to 24-hour urinary protein excretion rate.**[10]** The current study was conducted among CKD patients with different stages, the stage 3 and 4 patients to analyse the reliability of Spot UP/C ratio as a measure of proteinuria by comparing with the 24-hour urine protein estimation. In this study, the Correlation coefficient (r) between Spot UP/C ratio and 24-hour urine protein with the data transformed to a logarithmic scale was 0.641(P<0.05). Therefore, we found a significant positive correlation between 24-hour Urine protein and UPCR among CKD cases.

In a study done by Nayak R et al[10] on accuracy of spot urine protein creatinine ratio in measuring proteinuria in chronic kidney disease stage 3 and 4, it was found that Spot UP/C ratio predicted 24 hour Urine Protein with good accuracy (Correlation co-efficient, r = 0.86) on a data transformed to a logarithmic scale, P < 0.001, assessed In the same way Chitalia VC et al[11] in a prospective cross sectional study, which was performed on 170 patients with various glomerular abnormalities, to assess the accuracy of predicting 24-hour proteinuria from the spot urine protein creatinine ratio, observed a high positive correlations (r = 0.97) between UPCR and 24-hour proteinuria. Most of the differences between the two methods fell within the clinical limits of agreement.

In a longitudinal study by Antunes VV et al,[12] to study the diagnostic accuracy of the protein/creatinine ratio in urine samples to estimate 24-h proteinuria in Porto Alegre RS Brazil. There was observed that, the significant positive correlation between 24 hr Urine protein and the UPCR (P <0.001, k coefficient-0.86). Levels of agreement expressed in terms of Kappa coefficients. In our study UPCR had poor sensitivity and specificity in diagnosis of CKD stage 3, but found good sensitivity (90%) in diagnosis of CKD Stage 4. In our study, the 24 hours urine protein estimation had poor sensitivity and specificity in diagnosis of CKD stage 3 as compared to CKD Stage 4 (sensitivity=90%). The area under the curve was near to 1 in the ROC curve, for both the UPCR and 24 hours urine protein, it shows that UPCR can be a better predictor of CKD stage 4. The observation was found in study done by Nayak R et al, where in the

Area under the curve of ROC analysis was found to be close to 1, indicating that it's a appropriate test to detect proteinuria >150 mg/ 24 hour.[10]

An another study done by Patil P,[13] to evaluate and standardise the method of spot urine protein creatinine ratio (UP/C) for estimation of proteinuria. This study includes 241 study participants in a tertiary care hospital at Mumbai. In that study, the UP/C ratio of 0.1171 was correlated with 24 hours urine total protein equivalent of >150 mg/24 hrs with sensitivity 100%, specificity 98.1% (ROC curve).

Another important observation found in this study was that UPCR also had high predictive value for rate of decline of the glomerular filtration rate (P <0.05) in the stages 3, 4 and 5th stage of Chronic kidney disease. There is negative correlation(r=-0.302) between Urine Protein Creatinine ratio and eGFR. The level of negative correlation of UPCR with eGFR was found to be of higher than with that of 24-hour urine protein(r=-0.280). There we found that, the Significant positive correlation(r=0.279) was observed between UPCR and Creatinine.

In a same type of cross sectional longitudinal study, done by Ruggenenti P et al[14] in Bergamo, Italy, among 177 patients with chronic kidney disease, UPCR was found to have positive predictive value for the rate of decline of eGFRP = 0.0003) and end stage kidney failure (P = 0.002). As per multivariate Analysis report, the UPCR was the only variable significantly predicts the faster decline of GFR when compared to 24-hour urine protein. The protein: creatinine ratio on a random urine specimen gives an evidence to rule out the presence of significant proteinuria.[14,15,16,17,18] There are Systematic differences among urine ACR and AER, which are related to sex and other factors of muscle mass. The use of ACR versus AER gives different results in classification of albuminuria and changes in albuminuria status over period of time. These findings help us to ascertain methods over time, to standardize and optimally interpret measurement of urine albumin excretion in CKD cases. A greater benefit of the low blood pressure intervention was found in patients with higher baseline urine protein.[18,19,20,21]

CONCLUSION

The UPCR was found to have a higher predictive value for assessment of decline of glomerular filtration rates in the different stages of CKD than the 24 hours urine protein. Therefore, the UPCR is non-inferior to 24 hours protein estimation in assessing the function of kidney in CKD cases. So UPCR is a simple and cost-effective test in establishing the severity of Chronic kidney diseases and to predict the prognosis.

List of Abbreviations

CKD-Chronic kidney disease, UPCR-Urine protein creatinine ratio. GFR-Glomerular filtration rate, AER-Albumin excretion rate, ACR-Albumin creatinine ratio.

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