ISSN 2394–806X (Print), ISSN 2454-5139 (Electronic)
IJHRMLP, Vol: 03 No: 02 July, 2017
Printed in India
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ORIGINAL PAPER

Comparison of Spot Urine Protein-Creatinine Ratio With 24-hour Urine Protein in Glomerular Disease

Mahanta Pranab Jyoti[1], Goel Rohit[2], Mahanta D Monmoyuri[3]

***Received** on April 08, 2016; **editorial approval** August 08, 2016*

ABSTRACT

***Background:** The protein/creatinine (P/C) ratio in urine samples has been used in the clinical management of patients with glomerular diseases. The aim of this study is to evaluate the correlation between the Spot urinary Protein/Creatinine ratio and 24 hour urinary protein in patients with glomerular disease. **Methods:** It was a single centre, cross sectional study, conducted in Gauhati medical college and Hospital from July 2013 to June 2014. Patients admitted in department of nephrology due to glomerular disease were included for study. The relationship between the urine P/C ratio and the 24-hour protein excretion was assessed with the Pearson's correlation test. **Result:** A total 70 patients were enrolled for the study. Among them, 27 were males. The mean age of patients was 35.47 ±10.96 years. The most common glomerular disease was Systemic Lupus Nephritis (SLE, 25 cases). There was a significant correlation between 24 hour urine protein and spot urine protein ratio (P/C) ratio (correlation coefficient = 0.93, P < 0.001). **Conclusion:** This cross-sectional analysis corroborates the findings of previous studies, supporting the use of the spot urine protein ratio (P/C) ratio as an accurate test to define critical levels of proteinuria in patients with glomerular diseases.*

***Keywords:** Glomerular Disease, Proteinuria, Spot urine protein/ creatinine ratio*

INTRODUCTION

Proteinuria is a well-known marker for renal disease.[1] It is the most important test for both the initial evaluation and follow-up of patients with glomerulopathies. Dipstick tests are not clinically useful, since they have a low specificity and sensitivity for the detection and quantification of proteinuria.[2] Urine protein can be measured in random samples, in timed or untimed overnight samples, or in 24 hour collections. Protein excretion in a 24-hour urinary collection remains the reference (gold standard) method but subject to error due to over collection or under collection of urine. An alternative method for quantitative evaluation of proteinuria is the measurement of protein-to-creatinine ratio (PCR) in an untimed spot urine specimen, which provides a more convenient method to assess protein excretion.[1]

There is a high degree of correlation between 24-hour urine protein excretion and protein/creatinine ratios in random, single-voided urine samples in patients with a variety of kidney diseases.[3] It has been suggested that a protein/creatinine ratio of more than 3.0 or 3.5 mg/mg or less than 0.2 mg/mg indicates protein excretion rates of more than 3.0 or 3.5 g/24 hours or less than 0.2 g/24 hours, respectively.[3] However, only few studies have systematically examined the sensitivity and specificity or defined optimal levels of detection for protein/creatinine ratios in large numbers of patients with glomerular disease.

So, the purpose of this study is to evaluate the correlation between the Spot urinary Protein/Creatinine ratio and 24 hour urinary protein in patients with glomerular disease.

MATERIAL AND METHODS

It was a single centre, cross sectional study. Patients admitted in department of Nephrology from July 2013 to June 2014 with various glomerulopathies, were enrolled for study. Patients with age between 18 and 60 year, eGFR > 60 ml/min/1.73 m^2 (calculated from MDRD study equation, four-variable) and with proteinuria 1+ and above in urine by dipstick method were included for

Address for correspondence:
[1]Assistant Professor **(Corresponding author)**
Department of Nephrology
Mobile: +9109864067625
Email: pjmahanta@yahoo.com
[2]Senior Resident, Department of Nephrology- 781032
Gauhati Medical College and Hospital, Guwahati
[3]Associate Professor of Anatomy, Guwahati medical College, Guwahati

study. Those patients with eGFR < 60 ml/min/1.73 m^2, with febrile illness, urinary infection and gross hematuria and not giving consent for study were excluded.

Urine collection method was explained in detail to the patients to collect 24h and spot urine. All the subjects were instructed to begin the 24 hour collection immediately after completion of the first voiding in the morning and to collect all urine for 24 hours, including the final void at the completion of the 24 hour period. After discarding the first urine of the next day (which was included in the 24-hour urine sample), 3-5ml of urine was collected in the second sample for calculating the P/C ratio, which was calculated by dividing the proteinuria (mg/dl) of urine creatinine (mg/dl). Measurements on the 24-hour urine sample and spot urine protein & creatinine were performed on the same day as collections were completed. The adequacy of the 24-hr urine collection was assessed by comparing the total urinary creatinine in the sample with the predicted creatinine.

Creatinine concentration (mg/dl) was determined on a Vitros 350 Chemistry System (Ortho Chemical Diagnostic) with the modified Jaffe method. Protein concentration (mg/dl) was determined with a Vitros 350 Chemistry System Analyzer (Ortho Chemical Diagnostic) by biuret colorimetric assay. The urine protein: creatinine ratio was obtained by dividing the urinary protein concentration by the urine creatinine concentration (as this results in a ratio rather than an absolute number, SI units have not been used). Glomerular filtration rates (GFR) were calculated by the modification of diet in renal disease (MDRD – four variables) equation.

Statistical analysis: The correlation between P/C ratio in spot urine samples and urinary protein excretion in 24-hour collections were analyzed. The relationship between the urine P/C ratio and the 24-hour protein excretion was assessed with the Pearson's correlation test. Descriptive statistics were used for demographic and baseline data and summarized as mean ± standard deviation and percentage, where appropriate. A *p* value less than 0.05 were considered significant. The SPSS software (Statistical Package for the Social Sciences, version 19.0, SPSS Inc, Chicago, Ill, USA) and the Analyse-it software (version 9.60) were used for the analyses.

The study protocol was reviewed and approved by institutional ethics committees and patients written consents were obtained.

OBSERVATION AND RESULLT

A total of 70 patients were enrolled for the study. The mean age of the patients in the study was 35.47 ±10.96 year (19-59 year). Among the 90 patients who presented with proteinuria, 27 patients (38.5%) were male and 43 (61.50%) were female. The male to female ratio was 0.63:1. Regarding the distribution of glomerular disease (primary or secondary), the most common cause of proteinuria was Systemic Lupus Nephritis (SLE, 25 cases), followed by Focal and Segmental Glomerulosclerosis (FSGS, 19 cases). The mean serum creatinine value of study population was 0.89±0.2 mg/dl. The mean eGFR was 92.59 ±28.96 mL/min/1.73m^2 (calculated from MDRD Equation). The mean 24 hour urinary protein of study population was 5.71 ±5.0 gm/day (0.43 to 19.6 gm/day). The mean Spot urine protein/creatinine (P/C) ratio was 5.57 ±5.37 (0.4 to 24.07). Table 1 shows demographic and laboratory characteristics of the patients.

Table 1 Demographic and laboratory data at presentation

Baseline Characteristic and Investigation	
Total number of Patients	70
Age (year, mean ± SD)	35.47 ±10.96
Male : Female Ratio	0.63:1.0
24 hr Urinary Protein (gm, mean ± SD	5.71 ±5.0
Protein/Creatinine Ratio (mean ± SD)	5.57 ±5.37
eGFR (ml/min/1.73m2)	92.59 ±28.96
Distribution of Glomeruler Disease (Number, %)	
FSGS	19 (27.15)
MGN	17 (24.29)
SLE	25 (35.71)
DN	9 (12.85)

The correlation coefficient (r) between 24 hour urine protein and spot urine protein ratio (P/C) ratio was 0.93 (0.87- 0.96, 95% CI) that is strategically significant (p < 0.001)[Fig 1].

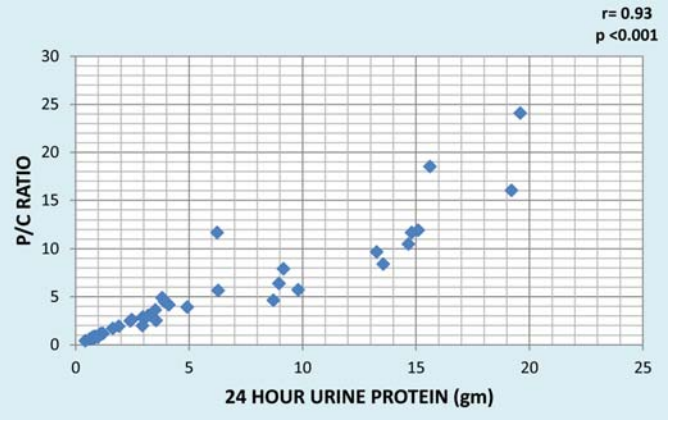

Figure 1 Scatter diagram showing correlation between 24 hour urine protein and spot urine P/C ratio among the entire samples (N=70)

DISCUSSION

An increase in urinary protein excretion is a widely accepted tool in the detection, diagnosis, and management of people considered to be at risk of developing renal disease and has been advocated as part of a regular check-up in such individuals.[4] The origins of this recommendation lie in the fact that, it is widely believed that there will be a change in the amount of protein excreted before any demonstrable change in glomerular filtration, for example, as reflected in the creatinine clearance.[5]

It is acknowledged that estimation of urinary protein excretion over a 24-h period is the reference, or gold standard method. This approach, however, is considered to be impractical in some circumstances, particularly in the outpatient setting, because of the difficulties associated with obtaining a complete collection. In a study of elderly patients, Mitchell et al.[6] had to discard

H”20% of the samples returned because they were considered to be incomplete. The need for a 24-h collection is a result of the high degree of variation in the urinary protein concentration during the course of the day. This variation in protein excretion is thought to be attributable to several factors, including (a) variation in water intake and excretion, (b) rate of dieresis, (c) exercise, (d) recumbency, and (e) diet. The variation may be further exacerbated by pathologic changes in blood pressure and renal architecture. This precludes the use of a shorter collection period or the use of a random urine sample for protein concentration measurements, a more practicable approach.

An alternative approach is that of expressing the protein excretion in a random urine collection, as a ratio to the creatinine concentration. It is assumed that both the protein and creatinine excretion rates are fairly constant during the day, as long as the glomerular filtration rate remains constant, and that is the major reason for changes in the protein concentration in individual samples during the day is variation in the amount of water excreted.[7] 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 and found that the mean intra-individual variation in the protein/creatinine ratio was 38.6%, whereas that of the protein excretion was 96.5%. Koopman et al.[8] had made a similar observation.

When treating patients with glomerulopathies, with or without nephrotic syndrome, the clinical goal is to normalize or at least to reduce proteinuria. Therefore, in clinical practice the absolute level of proteinuria in individual measurements is less important than its modification and reproducibility over time as a result of therapeutic interventions. In this context, assuming that reproducibility of the P/C ratio since initial diagnosis is adequate, it can be said that significant reduction in the P/C ratio means reduction in protein excretion, even if absolute values cannot be estimated with optimal accuracy[4]. For detection of these levels of proteinuria, the P/C ratio presented a high level of accuracy. Two previous studies[9,10] used the P/C ratio cut-off values of 0.2 and 3.5 in patients with various nephropathies and stable renal function to establish the diagnosis of pathologic proteinuria (P24 e”0.2 g) and nephrotic range proteinuria (P 24e”3.5 g), respectively. Our study also suggest a strong correlation ($r = 0.93$, $p<0.001$) between the P/C ratio and 24 hour protein like other previous studies. Our findings are in support to use of spot urine P/C ratio in clinical practice due to the simplicity of collecting the sample and its low cost.

Main limitation in our study is the number of patients studied, since it was less, sub-group analysis based on patient age, gender and the level of renal function (represented as eGFR) was not done. Increasing the number of samples collected and perhaps stratifying by underlying kidney disease would help us to acquire a better knowledge of the correlation between the two techniques studied.

CONCLUSION

The study concluded a good correlation between the results of 24 hour urine protein and spot urine protein/creatinine (P/C) ratio in assessment of proteinuria for patients with glomerular diseases. Thus, the random urine measurement might reduce the numbers of unnecessary 24-h urine collections and their associated unreliability. Future studies with large sample size, focused on monitoring patients with proteinuria, can be useful for evaluating the efficiency of the P/C ratio in detecting and monitoring of the underlying renal disease.

Acknowledgement: We express our gratitude to former Head of the department of Nephrology Dr. Anup Kr Barman, for encouragement for the study.

Conflict of interest: None.

Ethical clearance: Taken.

Source of funding: Node.

Contribution of Authors: We declare that this work was done by the author(s) named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors”. The first author and second author conceived, designed the study and third author analysed the data.

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