



INVESTIGATING THE ROLE OF SPOT URINE PROTEIN-TO-CREATININE RATIO IN PROTEINURIA ASSESSMENT

Clinical Biochemistry

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ABSTRACT

Proteinuria is the earliest and most sensitive indicator of renal disease. The standard method for the quantitative evaluation of proteinuria is the measurement of protein excretion in a 24-hour urine collection. However, it is cumbersome and often inaccurate due to over or under-collection. This study evaluated the correlation of spot urine protein-to-creatinine (P/C) ratio with varying degrees of 24-hour urine protein. **Methods:** This prospective study was conducted in patients with proteinuria at the Department of Nephrology, King Edward Memorial (KEM) Hospital, Mumbai. The 24-hour urine samples and spot urine samples were collected from all the patients included in the study. Urinary protein concentration was estimated by Trichloro Acetic acid (TCA) Ponceau-S dye method, whereas urine creatinine was estimated by the Jaffe's rate reaction method. The 24-hour urine protein was analyzed according to the degree of proteinuria. **Results:** 625 patients were included and 929 urine samples were analyzed in the study. Most patients belonged to the age group of 31-40 years. A significant correlation between 24-hour urine protein and spot urine P/C ratio was observed in the 24-hour proteinuria range of 0.151-0.300 g/day ($r=0.370$, low degree of correlation, $p<0.01$), 0.301-0.800 g/day ($r=0.457$, moderate correlation, $p<0.01$), 0.801-3.5 g/day ($r=0.668$, strong correlation, $p<0.01$), and 3.501-8.0 g/day ($r=0.50$, moderate correlation, $p<0.01$). **Conclusion:** The spot P/C ratio significantly correlated with 24-hour urine protein in the range of 0.3 g/day to 8.0 g/day. This confirms the use of the spot urine P/C ratio as a substitute for the 24-hour urine collection for the quantitative assessment of proteinuria.

KEYWORDS

Proteinuria, protein to creatinine ratio, spot urine, renal disease

INTRODUCTION

Proteinuria is an important indicator of renal dysfunction and has significant prognostic value in assessing the progression and prognosis of renal diseases [1]. Assessment of proteinuria content aids in diagnosing renal diseases and gauging the effectiveness of the applied treatment [2]. Higher level of proteinuria identifies patients with chronic kidney disease (CKD) who are at a higher risk of CKD progression and cardiovascular comorbidities [1].

The standard method for quantitatively evaluating proteinuria involves measuring protein excretion in a 24-hour urine collection [3]. Although it enables the consideration of daily protein variations and day-to-day readings, this method is time-consuming, inconvenient, and sometimes inaccurate [2]. An alternative method for quantitatively evaluating proteinuria is measuring the protein-to-creatinine (P/C) ratio in a spot urine specimen. This method is encouraged by the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (NKF KDOQI) guidelines, which offer a more practical way to evaluate protein excretion [4]. The P/C ratio in assessing 24-hour proteinuria is based on the fact that urine protein and creatinine excretion are reasonably constant in a stable glomerular filtration rate (GFR) [5].

The correlation between spot urine P/C ratio and 24-hour proteinuria has been well reported with varying levels of eGFR. However, there is a scarcity of studies that determine whether this correlation varies in accordance with different levels of proteinuria. Therefore, the present study aimed to evaluate the correlation of spot urine P/C ratio with varying degrees of 24-hour urine protein using narrow range of 24-hour urine protein.

METHODS

Study design

This prospective Observational study was conducted at the Department of Nephrology, King Edward Memorial (KEM) Hospital, Mumbai. Ethical approval was obtained from the KEM Institutional Ethics Committee (Approval no. 1102008) prior to the study

commencement. Written informed consent was obtained from all the patients involved in the study.

Inclusion and exclusion criteria

Patients aged 18-75 years, either of sex, with varying degree of proteinuria by dipstick and Sulphosalicylic acid (SSA) test, and those with varying degree of renal function were included in the study. Patients with urinary tract infections, congestive cardiac failure, post contrast administration, dehydration, and febrile illness were excluded.

24-hour and spot urine collection

Patients were instructed to void their first-morning urine sample and record the time. Subsequently, urine was collected for the next 24 hours from the time recorded. For 24-hour urine sample collection, patients were asked to collect urine in a 5 Litre container without adding preservative. On arriving at the laboratory, with 24-hour sample, patients were provided with a separate container for collecting spot urine sample.

Procedure

Protein and creatinine contents were analyzed in both 24-hour and spot urine samples by using a semi-automatic biochemistry analyzer, Secomam. Urinary protein concentration was detected by the TCA Ponceau-S dye method, whereas urine creatinine was estimated by the Jaffe's rate reaction method.

Protein analysis

The 24-hour urine protein was expressed in g/day and analyzed according to the degree of proteinuria as <0.150 g/day, 0.151-0.300 g/day, 0.301-0.800 g/day, 0.801-3.5 g/day, 3.501-8.0 g/day, and >8.0 g/day.

Statistical analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS) software, version 16.0. The association between 24-hour urine protein and spot urine P/C ratio was calculated using Karl Pearson's

correlation coefficient. P value <0.01 was considered statistically significant.

RESULTS

A total of 625 patients satisfying the eligibility criteria were included. Nine hundred and twenty-nine urine samples were used for analysis in the study. Table 1 depicts the age and gender distribution of the patients in the study. The proportion of male (51.6%) and female (48.4%) patients were comparable in the study. Mean [SD] eGFR was 57.25 [31.08] ml/min/1.73m². Overall, the majority of patients belonged to the age group of 31-40 years

Table 1: Age and gender distribution

Age groups (years)	Male (n=479)	Female (n=450)	Total (N=929)
18-20	47 (9.8)	30 (6.7)	77 (8.3)
21-30	107 (22.3)	111 (24.7)	218 (23.5)
31-40	89 (18.6)	163 (36.2)	252 (27.1)
41-50	104 (21.7)	92 (20.4)	196 (21.1)
51-60	88 (18.4)	39 (8.7)	127 (13.7)
61-70	30 (6.3)	10 (2.2)	40 (4.3)
>70	14 (2.9)	5 (1.1)	19 (2.0)

Data presented as n (%).

Maximum samples [403] were from patients who had nephrotic syndrome (Table 2).

Table 2: Underlying etiology of patients

Diagnosis	Number of sample (N=929)
Nephrotic syndrome	403 (43.4)
Chronic kidney disease	207 (22.3)
Diabetes mellitus	112 (12.0)
Lupus nephritis	68 (7.3)
Renal transplant	90 (9.7)
Others	49 (5.3)

Data presented as n (%).

Others: acute kidney injury, autosomal dominant polycystic kidney disease, hypertension, rapidly progressive glomerulonephritis.

Table 3: showing correlation of different degree of 24 hr. urine Protein with spot urine Protein to creatinine ratio

24hr protein g/day	Mean 24hr urine protein (SD)g/day		Spot urine P/C
<0.15 g/day	0.100(0.029)	Mean(SD) r p value<	0.144(0.115) 0.171 0.05
0.151 - 0.300 g/day	0.208(0.44)	Mean(SD) r p value <	0.226(0.164) 0.370 0.01
0.301 - 0.800 g/day	0.545(0.148)	Mean(SD) r p value <	0.69(0.521) 0.457 0.01
0.801 - 3.5 g/day	1.799(0.752)	Mean(SD) r p value <	2.131(1.259) 0.668 0.01
3.501 - 8.0 g/day	5.027(1.185)	Mean(SD) r p value <	5.25(2.207) 0.505 0.01
>8.0 g/day	10.114(1.494)	Mean(SD) r p value <	10.84(3.916) 0.22 0.05

Table 3: shows the correlation between different degrees of 24-hour urine protein and spot urine P/C ratio. 107 patients had 24-hour urine protein of 0.151-0.300 g/day, with a low degree correlation between 24-hour urine protein and spot urine P/C ratio in these patients ($r=0.370$, $P<0.01$). There were 149 patients with 24-hour urine protein of 0.301-0.800 g/day, demonstrating a moderate correlation with spot urine P/C ratio ($r=0.457$, $P<0.01$).

Moreover, a strong correlation was also observed between 24-hour urine protein and spot urine P/C ratio in the proteinuria range of 0.801-3.5 g/day ($n=407$; $r=0.668$), and moderate correlation in the range 3.501-8.0 g/day ($n=120$; $r=0.50$) ($P<0.01$, each).

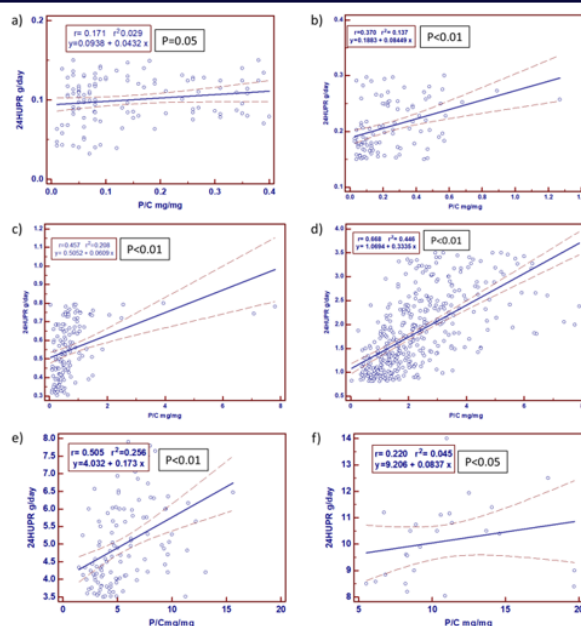


Figure 1: Scatter diagram showing correlation between a) 24-hour urine protein <0.150 g/day and spot urine P/C ratio ($n=120$), b) 24-hour urine protein 0.151-0.300 g/day and spot urine P/C ratio ($n=107$), c) 24-hour urine protein 0.301-0.800 g/day and spot urine P/C ratio ($n=149$), d) 24-hour urine protein 0.801-3.5 g/day and spot urine P/C ratio ($n=407$), e) 24-hour urine protein 3.501-8.0 g/day and spot urine P/C ratio ($n=120$), f) 24-hour urine protein >8.0 g/day and spot urine P/C ratio ($n=26$)

DISCUSSION

Measurement of urinary protein excretion is crucial for the diagnosis, prognosis, and treatment of renal disorders [6]. The most common technique employs a urine specimen collected over a 24-hour period to estimate the urine protein [5]. However, urine collection for 24 hours is inconvenient, and the process is prone to errors and inaccuracy. Therefore, the P/C ratio in spot urine specimens is used as a diagnostic alternative for quantitatively evaluating proteinuria [7]. The current study evaluated the correlation of spot urine P/C ratio with varying degrees of 24-hour urine protein.

In this study, most patients (27.1%) belonged to the age group of 31-40 years. A similar distribution was reported by Ahmed PI et al., [8] where 31.3% of patients with glomerulonephritis fell into the age group of 31 to 40 years. Another study conducted by Garg et al. also observed a higher proportion of patients in the age group of 31-40 years while investigating [5] the correlation between PC ratio and 24-hour urinary proteinuria among patients with different renal diseases.

In the present study, majority of patients had nephrotic syndrome (43.4%) of the patients. In this study, urine samples were categorized based on the degree of proteinuria, regardless of the severity of renal impairment. The study inculcated a narrow range of 24-hour proteinuria levels, specifically <0.150 g/day, 0.151 to 0.300 g/day, 0.301 to 0.800 g/day, 0.801 to 3.500 g/day, 3.501 to 8.0 g/day and >8.0 g/day. A significant correlation was found between the spot urine P/C ratio and 24-hour urine protein excretion across the range of proteinuria from 0.3 g/day to 8.0 g/day ($P<0.01$). However, correlation at proteinuria 0.151 g/day to 0.3 g/day though showing low level of correlation, was still statistically significant. No significant correlation was observed between spot urine P/C ratio and 24-hour urine protein excretion of <0.151 g/day ($P=0.05$) and >8.0 g/day ($P<0.05$). On similar lines, Ahmed PI [8] reported that significant positive correlation was observed between 24-hour urine protein and P/C ratio in patients with different ranges of 24-hour proteinuria, <0.2 g/day ($r=0.721$, $P<0.001$), 0.2-1 g/day ($r=0.788$, $P<0.001$), 1-3.4 g/day ($r=0.688$, $P<0.001$), and 3.5-6 g/day ($r=0.728$, $P<0.001$). However, no correlation was found between 24-hour urine protein and P/C ratio in patients having 24-hour proteinuria >6 g/day ($r=0.092$, $P<0.734$). A study conducted by Siu WK, et al. [9] showed that the spot urine P/C ratio correlated well with 24-hour urine protein excretion in patients with 24-hour proteinuria <3 g/day ($r=0.87$, $P<0.0001$). Moreover, a

significant correlation was demonstrated between spot urine P/C ratio and 24-hour urine protein excretion among patients with 24-hour proteinuria <1 g/day ($r=0.83$, $P<0.0001$). Another study [7] demonstrated a significant correlation between 24-hour urine protein and spot urine P/C ratio in the stratified degrees of 24-hour proteinuria <0.3 g/day ($r=0.498$, $P<0.001$), $0.3-3.499$ g/day ($r=0.828$, $P<0.001$), and ≥ 3.5 g/day ($r=0.181$, $P=0.420$), respectively.

CONCLUSION

The spot urine P/C ratio significantly correlated with 24-hour urine protein in the range of 0.3 g/day to 8.0 g/day. However, there was a no significant correlation of spot urine P/C ratio with very high proteinuria (>8.0 g/day) and very low proteinuria (<0.150 g/day). These findings suggest that the P/C ratio can be a reliable alternative to the 24-hour urine collection method for majority of the patients. It will help in quantitatively assessing proteinuria and defining critical levels of proteinuria accurately.

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