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Original Research Article

Evaluation of random urine sample protein: creatinine ratio as an index of 24 hour urine protein in patients with various renal disorders in tertiary care center

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ABSTRACT

Background: Commonly used methods to measure protein are 24 hours urine collection, which is time consuming cumbersome and often in accurate, the other method, infrequently used, is estimation of proteinuria from protein-creatinine ratio. The objective of the study was to compare spot urine protein-creatinine ratio with 24 hours urine protein as an index of quantitative proteinuria.
Methods: 110 patients with persistent dipstick positive proteinuria with varying degrees of renal dysfunction were included in this study. First morning spot urine sample were used to estimate protein creatinine ratio and then 24 hours urine protein estimation was done and compared.
Results: There was significant correlation between 24 hours urine protein and protein creatinine ratio ($r = 0.70$) ($P<0.01$) However maximum correlation was in patients with normal or mild renal dysfunction and non nephrotic range proteinuria ($r = 0.92$) ($p<0.01$).
Conclusions: Protein creatinine ratio in a spot morning urine sample is a precise indicator of proteinuria and represents a simple and inexpensive procedure in establishing severity of proteinuria.

Keywords: Protein preatinine ratio, Proteinuria, Random urinary protein, Urine analysis

INTRODUCTION

Persistent proteinuria of >1.0 gm/day usually indicates renal disease.Proteinuria may be minimal (<1.0 gm/day), moderate (1-3 gm/day) and heavy (>3 gm/day). Important causes of minimal proteinuria are chronic pyelonephritis, diabetic nephropathy, interstitial nephritis and chronic renal failure. Moderate proteinuria is seen in nephritic syndrome and toxic nephropathies and heavy proteinuria indicates active glomerulonephritis. So quantification of protein is very important.[1] Current methods for measuring proteinuria vary significantly. Commonly used methods are dipstick urine analysis, 24 hours urine protein estimation and spot urine protein Creatinine ratio.

METHODS

Total of 110 patients, with persistent dipstick positive proteinuria, admitted in Nephrology and medical wards of Osmania general hospital were included in this study over 2 years. Patients of either sex, aged above 14 years, with persistent dipstick positive proteinuria (on 2 different occasions at least 1 week apart) were included. Patients with age less than 14 years, with gross hematuria, with febrile illness, dehydration, head injury, cardiac failure were excluded. A detail history of the illness, general physical examination and systemic examination was done.

Patients were advised to give their first morning urine sample for estimation of urine protein creatinine ratio. Then for the estimation of 24 hours urine proteins, these patients were provided with plastic can (5 liters capacity) to collect their 24 hours urine. The time was noted and patient was advised to collect their entire 24 hours urine in the can provided to them, including the last void urine at the end of 24 hours.

The urine for 24 hours protein and spot protein concentration was estimated by using dye binding technique with pyrogallol red in DADE BEHRING auto analyzer. Spot Urine for creatinine was estimated by using modified Jaffe's method in DADE BEHRING auto analyzer.

Patients were divided into 2 groups depending on creatinine clearance. Creatinine clearance was estimated from age, sex, weight and serum creatinine of the individual by the following formula of Cockcroft Gault.[2] Patients were categorised into two groups as follows:

Group 1: Calculated Creatinine clearance >50 ml/min.

Group 2: Calculated Creatinine Clearance <50ml/min.

Each group was further divided into two sub groups depending on degree of proteinuria.

Group 1 A: Calculated creatinine clearance >50ml/min and nephrotic range proteinuria (>3.5 gm/day).

Group 1 B: Calculated creatinine clearance >50ml/min and non nephrotic range proteinuria (<3.5 gm/day).

Group 2 A: Calculated creatinine clearance <50ml/min and nephrotic range proteinuria (>3.5 gm/day).

Group 2 B: Calculated creatinine clearance <50 ml/min and non nephrotic range proteinuria (<3.5 gm/day).

RESULTS

This study included 110 patients, who had persistent proteinuria with varying degree of renal dysfunction, admitted in nephrology and medicine wards of Osmania general hospital. The patients were segregated in to four groups depending on calculated creatinine clearance and degree of proteinuria. The results were tabulated and analysed as shown in Table 1.

Table 1: Age distribution of patients with proteinuria.

Age in years	Number of patients	Percentage
<20 years	8	7.27%
20-40 years	31	28.18%
40-60years	44	40%
>60 years	27	24.54%

In this study the age ranged from 15 to 90 years. The incidence of proteinuria was maximum in the age group of 40-60 years (40%).

Table 2: Comorbid conditions in patients with proteinuria.

Comorbid conditions	Number of patients	Percentage
Hypertension	74	67.27%
Diabetes mellitus	62	56.36%
Chronic kidney disease	56	50.9%
Ischemic heart disease	18	16.3%
Stroke	6	5.45%
Systemic lupus erythematosis	6	5.45%

This study showed that diabetes and hypertension were the commonest comorbid illness associated with proteinuria as shown in Table 2.

Table 3: Classification of patients based on degree proteinuria.

Proteinuria	Number of patients	Percentage
Nephrotic (>3.5 gm/day)	44	40
Non Nephrotic	66	60

Out of the 110 patients with persistent proteinuria, 44 patients (40%) had proteinuria of more than 3.5 gms/24 hours and 66 patients (60%) had proteinuria less than 3.5 gms/24 hours as given in Table 3.

Table 4: Segregation of patients into different groups.

Calculate creatinine	Nephrotic	Non nephrotic
Clearance	Protinuria	Proteinuria
>50 m/min	6 (Group 1A)	24 (Group 1B)
<50 m/min	38 (Group 2A)	42 (Group 2B)

In this study 38 patients had moderate to severe renal dysfunction with nephrotic range proteinuria. There were 42 patients with moderate to severe renal dysfunction and non nephrotic range proteinuria. 24 patients had normal to mild renal dysfunction with non nephrotic range proteinuria and 6 patients had normal to mild renal dysfunction with nephrotic range proteinuria as shown in Table 4.

Table 5: Correlation co-efficient.

Groups	Correlation co-efficient (r)
1 A	0.6673
1 B	0.9251
2 A	0.5297
2 B	0.1974

In the four groups studied there was good correlation between spot urine protein creatinine ratio and 24 hours urine protein. The correlation was best in patient with creatinine clearance >50 ml/min and non nephrotic range proteinuria (r = 0.9251), the correlation was least in patient with creatinine clearance <50 ml/min and non nephrotic range proteinuria as shown in Table 5.

DISCUSSION

Measurement of urinary proteins over 24 hours is the definitive method to quantify proteinuria. However, prolonged collections of urine are inconvenient and often inaccurate due to frequent collection errors.[3]The protein creatinine ratio of randomly obtained urine specimen correlated well with 24 hours urine protein with varying degree of proteinuria and normal to severely impaired renal functions. However the best positive correlation was in patients with non nephrotic proteinuria and normal or mildly impaired renal function (Group 1 B r = 0.92).

The positive correlation was least in patients with moderate to severe renal dysfunction and non nephrotic range proteinuria (Group 2 B r = 0.19). Rathi et al reported good correlation between protein creatinine ratio from a spot urine sample and daily urinary protein excretion rate.[4] Ginsberg et al studied that quantitation of urinary protein excretion is used extensively for diagnostic and prognostic purposes and to assess the effects of therapy.[3] In the presence of stable renal function, a protein/creatinine ratio of more than 3.5 (mg/mg) can be taken to represent "nephrotic-range" proteinuria, and a ratio of less than 0.2 is within normal limits. The randomly obtained urine protein creatinine ratio would be expected to predict 24hour protein for several reasons.[5]

First, the concentrations of protein and creatinine in the urine are determined by their excretion rates and by the tubular reabsorption of water. Since water reabsorption is the same for both values of the same specimen, the protein creatinine ratio therefore reflects the excretion rate of protein relative to creatinine. Second, when both urinary protein and urine creatinine values are reported in similar units (mg/dl), the protein creatinine ratio can be thought of as the excretion rate of urinary protein in grams relative to the excretion of 1 gm creatinine. Finally, since the average person excretes approximately 1 gm/day creatinine, the ratio there for can be directly used to estimate 24 hour urinary protein in grams/day. In this study most of the patients who had 24 hour proteinuria >3.5 gms had protein creatinine ratio of >3.5 in spot urine.

Out of the 36 patients in our study with a protein creatinine ratio of >3.5 g, 28 patients (77.7%) had nephrotic range proteinuria by 24 hours estimation. This is similar to 71-94% seen in other studies.[3,6,7] Sharma et al studied the correlation between the protein creatinine ratio in spot urine sample with 24 hours urine protein with varying degree of renal dysfunction and concluded a good positive correlation in patients with mild renal failure.[8] In this study there good correlation in mild renal failure compared to advance renal failure best positive correlation was in patients with non nephrotic proteinuria and normal or mildly impaired renal function (group 1 B r = 0.92). Positive correlation was least in patients with moderate to severe renal dysfunction (group 2 B r = 0.19).

Ruggenenti et al in his studies concluded that the 24 hours urine protein can be directly predicted from a random urine specimen by estimating protein creatinine ratio.[9] Vishwanathan et al concluded that estimated proteinuria calculated from urinary protein creatinine ratio in a random urine sample is useful in serial evaluation of kidney function on a follow up basis.[10]

CONCLUSION

There was good positive correlation between spot urine protein creatinine ratio and 24 hours estimated protein. The correlation was best in patients with normal or mildly impaired renal dysfunction with non nephrotic proteinuria. Urine protein creatinine ratio is easy to perform, inexpensive and less time consuming method for measuring of proteinuria. It can thus be used in the outpatient setting for screening and quantification of proteinuria.

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