COMPARATIVE ANALYSIS OF PROTEINURIA BY PROTEIN CREATININE RATIO AND 24 H URINARY PROTEIN EXCRETION IN RENAL PATIENTS
Leelavathi Venkatesh1, Kowsalya R.2

1Assistant Professor, Department of Nephrology, Institute of Nephrourology, Victoria Campus, Bangalore, Karnataka.
2Associate Professor, Department of Biochemistry, Institute of Nephrourology, Victoria Campus, Bangalore, Karnataka.

ABSTRACT

BACKGROUND
The Kidney Disease Outcomes Quality Initiative (K/DOQI) of the National Kidney Foundation Practice Guideline as well as American Diabetes Association (ADA) recommends spot urine protein creatinine ratio (UPCR) proteinuria to assess proteinuria. This study was undertaken to evaluate the correlation of UPCR with 24-hour urine for estimation of proteinuria in patients with different aetiology for renal failure.

METHODS
This retrospective study was conducted in tertiary care renal referral hospital between December 2018 and May 2019 Patients enrolled in the study were diagnosed with renal failure due to different causes. The patients with incomplete data, having oliguria and inadequate urine collection were excluded from the study. The urine protein and creatinine concentration of both 24 h and spot urine were evaluated.

RESULTS
Among 74 patients enrolled in the study, the majority of cases were diagnosed with diabetic nephropathy (48.60%), followed by IgA nephropathy (16.10%) and rest of the patients (35.30%) with other renal diseases. The mean 24 h urine protein concentration was 2270.68 mg/day. The mean spot urine creatinine concentration was 96.2 mg/dL and mean spot protein concentration was 197.97 mg/dL. UPCR and 24 h urine protein estimation had strong correlation with r = 0.846 and p < 0.001 with Pearson’s correlation analysis.

CONCLUSIONS
Spot/random UPCR is a reliable method to estimate urinary protein excretion. It can be an alternative to 24 h urine collection especially in renal patients particularly in children, elderly and pregnant women.

KEYWORDS
Kidney, diabetic nephropathy, IgA nephropathy, proteinuria, Pearson’s correlation, renal.

HOW TO CITE THIS ARTICLE: Leelavathi V, Kowsalya R. Comparative analysis of proteinuria by protein creatinine ratio and 24 h urinary protein excretion in renal patients. J. Evid. Based Med. Healthc. 2019; 6(38), 2554-2558. DOI: 10.18410/jebmh/2019/525

BACKGROUND
Proteinuria is a condition wherein protein excretion is greater than 150 mg per day and its quantification is a vital screening tool for diagnosis of renal diseases. It occurs in various circumstances from benign like stress, fever, exercise to serious diseases like glomerular nephritis, chronic kidney disease (CKD), diabetic nephropathy, multiple myeloma, rheumatic diseases etc., Proteinuria is not only useful in diagnosis, but also crucial in determining disease progression and management of renal diseases. Accurate identification and quantitation of proteinuria is pivotal. Urinary dipsticks and sulfosalicylic acid tests are older methods of proteinuria detection. These diagnostic procedures are inexpensive, easily available but non-quantifiable wherein their accuracy is a matter of concern. Later, 24 h urine collection method was introduced to detect urinary protein excretion. This method has certain drawbacks like greater time consumption, patient inconvenience, effect of circadian rhythm etc. However, currently random or spot urine protein/creatinine is a preferred method to assess protein excretion in clinical practice. This simple and convenient method is recommended by the Kidney Disease Outcomes Quality Initiative (K/DOQI) of the National Kidney Foundation Practice Guideline as well as American Diabetes Association (ADA) to assess proteinuria especially in staging of CKD. Most cases do not require timed urine sample to detect proteinuria except in conditions like diabetes necessitating detection of microalbuminuria or proteinuria, hence spot urine sample collection is more suitable. Hence the objective of our study was to evaluate the correlation of spot (random) urine protein creatinine ratio (UP/C) with 24-hour urine for estimation of proteinuria in patients with different aetiology for renal failure. This study postulates accurate
METHODS
This was a retrospective study conducted between December 2018 and May 2019 at the Institute of Nephro-Urology, a tertiary-care referral hospital. The obtained data was reviewed and checked for presence of 24h urine protein concentration, creatinine concentration, total volume, and most importantly, a concomitant analysis of the spot urine sample for Protein creatinine Ratio (PCR). The 24 h urine samples were collected in a container at home or at the ward using a Foley catheter or by self-voiding. The collected urine sample was transferred into a clean storage container and kept in a cool, hygienic environment. The urine protein and creatinine concentration of both 24 h and spot urine were both determined by the Abbott ci41000 Auto-analyzer.

This study was of retrospective type hence written informed consent from the patients could not be obtained. The patients with incomplete data, having oliguria (24 h urine volume less than 400 mL) and inadequate urine collection (insufficient 24 h urinary creatinine excretion per body weight) were excluded from the study. All the measurements were determined in a single central laboratory. UPCR was calculated from urine protein (mg/dL) divided by urine creatinine (mg/dL). 24 h urine protein excretion was used as the standard reference, which was calculated by urine protein (mg/dL) multiplied by 24 h urine volume (mL) and then converted and presented in gram/day. The percentage discrepancy between UPCR and 24 h urine protein excretion (24 h-UP) was calculated as (UPCR—24h-UP) ÷ 24h-UP × 100% to measure the diagnostic accuracy of UPCR.

Statistical Analysis
Values of the continuous variables are presented as mean. Pearson’s correlation coefficient and p value of less than 0.05 was considered to be statistically significant.

RESULTS
Out of 74 patients included in the study 55 (74.32%) were males and 19 (25.68%) were females with the mean age of 47 years. The demographic features and clinical parameters (Table 1), including age, gender, 24 h urine protein, creatinine, total volume was recorded. Serum laboratory data were obtained at the time of urine collection. Among 74 patients, majority of cases were of diabetic nephropathy 48.60% followed by with IgA nephropathy (16.10%). The remaining 35.30% patients were diagnosed with chronic interstitial nephritis, acute kidney injury, minimal change disease, cast nephropathy etc.

The mean 24 h urine protein concentration was 2270.68 mg/day, while the mean spot urine creatinine concentration was 96.20 mg/dL and mean spot protein concentration was 197.97 mg/dL. There was no significant difference seen with regard to disease progression and UPCR and 24 h protein excretion. In addition, the correlation degree (two-tailed p) of quantitative daily urine protein excretion between the 24 h and spot urine was examined. This showed a statistically significant finding with Rho=0.846 and p < 0.001. Figure 1 shows the correlation between protein/creatinine ratio and proteinuria.

DISCUSSION
Proteinuria is an important marker in determining the severity and progression of various renal diseases and cardiovascular disease. Numerous studies have been conducted to explore the correlation between UPCR and 24 h urine excretion in different renal issues like CKD, lupus nephritis, preeclampsia, kidney transplantation, Systemic lupus erythematosus. Table 2 summarizes studies (published after 2000) and reveals a good correlation between both the methods. These studies have been performed in renal patients of different aetiologies, pregnant women with preeclampsia and children as well. Although 24 h urine protein detection is an accurate method and gives a wide range of clinical data, UPCR is an ideal procedure with respect to convenience of patients and simplicity.10 This method is most appropriate in children, elderly and pregnant women wherein fast and less invasive technique is desired.11,12

The present data is obtained from a comparative study between UPCR and 24 h protein quantification. This study is a retrospective, cohort study with predominantly male population. The mean age of patients was 47 years. Majorly patients were having Diabetic nephropathy (48.60%) and IgA nephropathy patients (16.10%) being the second highest in number. Residual population (35.30%) having other renal diseases. 24 h urine protein excretion was used as a standard method to check for accurate collection of urine samples. The completion of 24 h urine collection is evaluated by urine creatinine excretion rather than volume measurement.

The current study shows correlation coefficient of 0.846 which is in accordance with the findings of Schwab et al, and of Ginsberg et al.13,14 Gai et al and Montero et al also reports spot urine protein to creatinine a better diagnostic tool for protein measurement in renal patients.15,16 Few previous studies have claimed a poor correlation between spot UPCR and 24 h urine collection method. Patients with extreme muscle mass and high protein excretion are prone to over or underestimation of protein excretion leading to false diagnosis of diseases.17-19 Akin et al found weakest correlation between the two methods in diabetes mellitus.20 This study was limited by its retrospective design and a relatively small sample size. Hence a bigger sample size studies are warranted. Another limitation is that these findings were based on a 24 h urine sample database. Finally, the spot urine cohort lacks the information of the urine collection time due to the retrospective nature of the study; however, the K/DOQI guideline recommended that random urine specimens are acceptable in the absence of first morning urine specimens.
CONCLUSIONS

Our study demonstrated a significant correlation between UPCR and 24 h urine protein estimation with \( r = 0.846 \) and \( p < 0.001 \) with Pearson’s correlation analysis. Thus spot/random UPCR is a reliable method to estimate urinary protein excretion. It is an appropriate alternative to 24 h urine collection in renal patients particularly in children, elderly and pregnant women where patient convenience is of prime importance.

REFERENCES


Figure 1. Linear Relationship between the Spot UPCR Test and 24 h Proteinuria in Renal Patients

Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Author et al.</th>
<th>Disease/Population</th>
<th>r</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Akin et al., 2019</td>
<td>Patients with glomerulonephritis, hypertension, diabetes, CKD</td>
<td>0.89</td>
<td>Not stated</td>
</tr>
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<td>2.</td>
<td>Rodeo-Haad et al., 2018</td>
<td>Kidney transplant</td>
<td>0.76</td>
<td>&lt; .001</td>
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<td>3.</td>
<td>Salinas et al., 2018</td>
<td>Preeclampsia</td>
<td>0.67</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>4.</td>
<td>Yang et al., 2017</td>
<td>Children</td>
<td>0.80</td>
<td>&lt; .001</td>
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<tr>
<td>5.</td>
<td>Hogan et al., 2016</td>
<td>Glomerular disease</td>
<td>0.90</td>
<td>Moderate</td>
</tr>
<tr>
<td>6.</td>
<td>Baba et al., 2016</td>
<td>Normotensive pregnant women</td>
<td>0.64</td>
<td>Not stated</td>
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<tr>
<td>7.</td>
<td>Ulibata et al., 2016</td>
<td>Nephropathy</td>
<td>0.76</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>8.</td>
<td>Medina-Rosado et al., 2015</td>
<td>Systemic lupus erythematosus</td>
<td>0.29</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>9.</td>
<td>Bhide et al., 2015</td>
<td>Suspected preeclampsia</td>
<td>0.86</td>
<td>&lt; .1</td>
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<td>10.</td>
<td>Zhang et al., 2015</td>
<td>Lupus nephritis</td>
<td>0.82</td>
<td>&lt; .001</td>
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<td>11.</td>
<td>Antonello et al., 2015</td>
<td>Nephropathy in HIV patients</td>
<td>0.957</td>
<td>Not stated</td>
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<td>12.</td>
<td>Montero et al., 2012</td>
<td>Renal disease</td>
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<td>&lt; .001</td>
</tr>
<tr>
<td>13.</td>
<td>Gao et al., 2012</td>
<td>Preeclampsia</td>
<td>0.94</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>14.</td>
<td>Cade et al., 2012</td>
<td>Preeclampsia</td>
<td>0.98</td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>15.</td>
<td>Matar et al., 2012</td>
<td>Lupus nephritis</td>
<td>0.91</td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>16.</td>
<td>Sethuram et al., 2013</td>
<td>Preeclampsia</td>
<td>0.82</td>
<td>Not stated</td>
</tr>
<tr>
<td>17.</td>
<td>Salesi et al., 2009</td>
<td>Systemic lupus erythematosus</td>
<td>0.83</td>
<td>&lt; .0001</td>
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<td>Shahbazian et al., 2008</td>
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<td>19.</td>
<td>Sendrorg E et al., 2008</td>
<td>Children</td>
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<td>20.</td>
<td>Antunes et al., 2008</td>
<td>Primary glomerulopathies</td>
<td>0.90</td>
<td>&lt; .001</td>
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<td>21.</td>
<td>Leung et al., 2007</td>
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<td>0.91</td>
<td>&lt; .0001</td>
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<td>22.</td>
<td>Zadehmdarin et al., 2006</td>
<td>Preeclampsia</td>
<td>0.70</td>
<td>&lt; .001</td>
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<td>23.</td>
<td>Gai et al., 2006</td>
<td>Nephropathy</td>
<td>0.82</td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>24.</td>
<td>Lane et al., 2006</td>
<td>Nephropathy</td>
<td>0.92</td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>25.</td>
<td>Christopher-Stine et al., 2004</td>
<td>lupus nephritis</td>
<td>0.89</td>
<td>Not stated</td>
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<td>26.</td>
<td>Al et al., 2004</td>
<td>Hypertensive pregnant women</td>
<td>0.56</td>
<td>&lt; .01</td>
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<td>27.</td>
<td>Yamasmit et al., 2004</td>
<td>Pre-eclampsia</td>
<td>0.95</td>
<td>&lt; .001</td>
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<tr>
<td>28.</td>
<td>Durwal et al., 2003</td>
<td>Pre-eclampsia</td>
<td>0.64</td>
<td>&lt; .0001</td>
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<td>29.</td>
<td>Chitale et al., 2001</td>
<td>Glomerular diseases</td>
<td>0.97</td>
<td>Not stated</td>
</tr>
<tr>
<td>30.</td>
<td>Torg et al., 2001</td>
<td>Renal transplant</td>
<td>0.79</td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>31.</td>
<td>Kim et al., 2001</td>
<td>Children</td>
<td>0.88</td>
<td>&lt; .001</td>
</tr>
</tbody>
</table>

Table 2. Reported Studies Summarizing Correlation Ratio of UPCR and 24 h Proteinuria


Zhang Q, Sun L, Jin L. Spot urine protein/creatinine ratio is unreliable estimate of 24 h proteinuria in lupus nephritis when the histological scores of activity index are higher. Lupus 2015;24(9):943-947.


