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UTILITY OF PROTEIN-CREATININE RATIO AND PROTEIN-OSMOLALITY RATIO IN PREDICTING PROTEINURIA IN KIDNEY TRANSPLANT RECIPIENTS.

Biochemistry

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ABSTRACT

Proteinuria is the most important diagnostic and prognostic marker in patients with different kidney diseases and in kidney transplant recipients as well. Quantitative estimation of 24-hour protein excretion is considered as a gold standard test for proteinuria. However, 24-hour collections are time consuming, cumbersome, and often inaccurate due to over or under collection. The excretion of creatinine and protein is reasonably constant throughout the day when glomerular filtration rate is stable. Spot urine protein to creatinine (P/C) ratio is recommended as an accurate method to determine proteinuria in adults and children. However urinary excretion is influenced by hydration-dehydration status of the patient. Excretion patterns of creatinine and protein may vary according to the severity and the type of kidney disease. This may affect the urinary P/C ratio. To overcome this problem protein to osmolality (P/O) ratio is assessed. The present study was conducted to compare and assess the validity of spot urine P/C ratioand spot urine P/O ratio in predicting 24-hour urine protein. **Method:** 90 samples (males-74, females-16) were processed. Protein estimation was done in 24-hour urine sample and spot urine samples were processed for protein, creatinine, and osmolality. Pearsons's correlation coefficient and simple linear regression analysis were used to assess the relation between 24-hour urine protein, spot urine P/C ratioand spot urine P/O ratio. The comparison and correlation between 24-hour urine protein and spot urine P/C and spot urine P/O ratio was studied. **Results:** For the entire dataset there was significant correlation between 24-hour urine protein and spot urine P/C ratioand spot urine P/O ratio at p value <0.001, with r= 0.797 and 0.724 respectively. **Conclusion:** Spot urine P/C ratio and spot urine P/O ratio are good predictors of 24-hour urinary protein.

KEYWORDS

Proteinuria, Spot urine P/C ratio, spot urine P/O ratio and 24-hour urine protein.

INTRODUCTION

Proteinuria is the marker of parenchymal damage and an important early prognostic marker of poor kidney outcome in many kidney diseases. [1,2,3] Kidney transplant recipients experience proteinuria due to many reasons like kidney transplant rejection, calcineurin inhibitor toxicity, recurrence of original disease, de novo glomerulonephritis.[4,5] Proteinuria results in a greater risk of poor graft outcome and mortality in kidney transplant recipients.[6,7] Accurate detection of urinary protein excretion is thus very important. Studies done in the early post-transplant period have shown that proteinuria from native kidney decreases after a successful transplant.[8] For kidney transplant recipients, the assessment of protein excretion can indicate treatable causes like early transplant glomerulopathy or recurrent glomerulonephritis. It is important to evaluate the utility of proteinuria in the management of kidney transplant recipients. 24-hour Protein estimation is the gold standard but, 24-hour collections are time consuming, cumbersome, and often inaccurate due to over or under collection. Short timed collections may reduce the inconvenience of 24-hour urine collections, but a slight error in the duration of collection period or missing sample of urine would be exaggerated several folds when values are interpreted in terms of 24-hour urine protein. Studies have shown that both protein to creatinine ratio [9,10,11] and protein to osmolality ratio [12,13] are a good marker of predicting 24-hour protein excretion in various diseases.The present study aims at comparing 24-hour protein estimation in urine with spot protein to creatinine (P/C) ratioand protein to osmolality (P/O) ratio.

MATERIALS AND METHODS

This prospective observational study was conducted at Department of Nephrology, King Edward Memorial Hospital (KEMH), Mumbai, India. Ethical approval was obtained from Institutional Ethics Committee, KEMH (Approval no. 1102008) prior to the study commencement. Written informed consent was obtained from all the patients involved in the study. All kidney transplant recipients above 18 years, with varying degrees of proteinuria were included. Patients with urinary tract infections, congestive cardiac failure, post contrast administration, dehydration, and those with fever were excluded.

Transplant recipients managed by the departmentand satisfying inclusion and exclusion criteria were recruited for this study. The patients were instructed to discard the first morning void and note the time. The subsequent voids were collected for 24 hours. Subjects were asked to collect 24-hour urine in a 5-litre can. No preservatives were added.At the time of submission of 24-hour urine sample to the laboratory, patients were asked to collect a spot urine sample and submit for examination.

24-hour samples were processed for protein and creatinine estimation. Spot urine samples were processed for protein, creatinine and osmolality estimation. Urine protein was estimated by TCA-Ponceau S Dye method on a semi-automatic biochemistry analyser (Secomam). The results obtained were expressed in mg/dl. Creatinine was estimated by Jaffe's rate reaction method on semi-automatic biochemistry analyzer (Secomam). The result obtained was expressed in mg/dl. Urine Osmolality was measured by means of freezing point depression method using osmometer (Advanced Instruments Model 3250). The results obtained were expressed in mOsmols/kg H_2O.

Statistical Analysis:

The statistical analysis was done using SPSS (Statistical Package for social sciences) Version 16 Software. The correlation of coefficient was calculated by using Karl Pearson's correlation coefficient.24-hour urine protein values were plotted against spot P/C ratio and spot urine P/O ratio. Correlation coefficient and simple linear regression analysis was used to assess relation between them. Mean, SD, Pearson correlation coefficient and p values were assessed.

RESULTS:

Out of 90 samples, 74 were from males and 16 from females. The mean age was 36.9 (+10.09) years. For the entire data set there was significant correlation between 24-hour urine protein and spot urine P/C ratio and spot urine P/O ratio with correlation coefficient ($p<0.001$) r = 0.797 and 0.724 respectively. From table 1 it is seen that

statistically significant correlation (p value < 0.001) was found between 24-hour urine protein and spot urine P/C and P/O in patients in kidney transplant recipients (r= 0.797,0.724 respectively)

Table 1 Correlation Between 24 hr. Protein And Spot Urine P/C And Spot Urine P/O

Mean 24-hour urine protein (SD) g/day		Spot urine P/C	Spot urine P/O
1.416 (0.933)	Mean (SD)	1.216(0.908)	0.289(0.235)
	r	0.797	0.724
	P value<	0.001	0.001

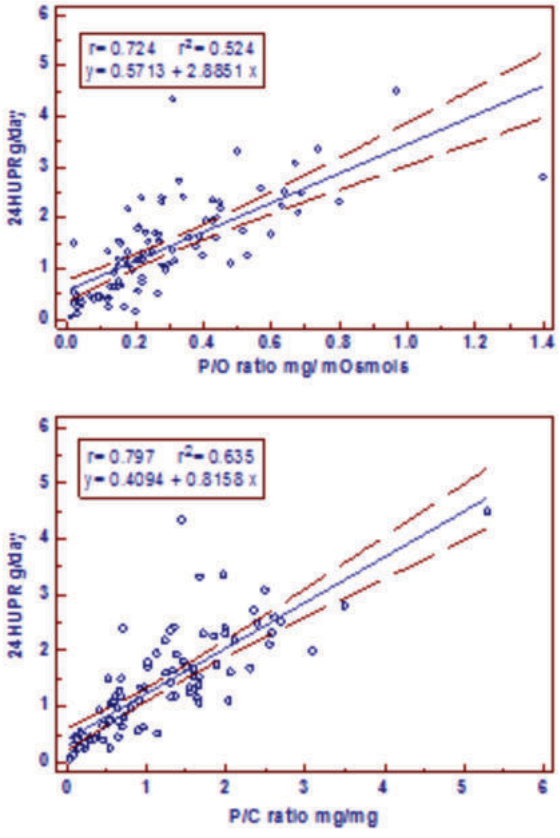

Fig 1a: Scatter diagram showing correlation between 24 hour urine protein and spot urine P/C in Transplant patients. (n=90) b: Scatter diagram showing correlation between 24 hour urine protein and spot urine P/O in Transplant patients. (n=90)

DISCUSSION

Early diagnosis of allograft injury remains one of the greatest challenges in kidney transplantation. Proteinuria is periodically measured in kidney transplant recipients for diagnosing allograft injury. It is an important predictor of both allograft failure and death in kidney transplant patients. (14-15) Proteinuria in the nephrotic range as well as low grade is associated with adverse kidney allograft outcome.[16] Due to the drawback of 24-hour collection, efforts have been made to quantify 24-hour urine protein by protein to creatinine (P/C) ratio and spot urine protein osmolality (P/O) ratio. The National Kidney Foundation (K/DOQI) guidelines stated that proteinuria can be accurately assessed by the use of spot urine P/C ratio. P/O ratio is another alternative to be used to estimate 24-hour urine proteinuria. P/O ratio has been studied in children with proteinuria [12,17] and has been found to be a good marker for predicting abnormal renal function in HIV-infected patients receiving tenofovir.[18]

The findings of this study showed a significant strong correlation between 24-hour urine protein and spot urine P/C ratio and spot urine P/O ratio with correlation coefficient ($p<0.001$) with $r = 0.797$ and 0.724 respectively. This is in agreement with findings from other studies performed in non-kidney transplant recipients. Hooman et al [17] showed that both urine P/O ratio and urine P/C ratio from random urine specimen are good predictors of 24-hour urinary total protein excretion. Morgenstern et al [13] studied random urine samples in children with proteinuria and concluded that the measurement of urine P/C ratio serve the purpose better than the P/O ratio to measure 24-hour protein excretion. But in adults both the ratios could equally and accurately measure the 24-hour protein excretion.

For P/O ratio we need an osmometer which may not be possible on a small set up. Urine P/C ratio is the best option for prediction of 24-hour protein in transplant patients, however this study shows that protein osmolality ratio can be used with comparable accuracy for this purpose as well.

CONCLUSIONS

In conclusion, our study shows that there is a significant correlation between 24-hour urine protein and spot P/C or P/O ratios, both of which can be used for estimating proteinuria in kidney transplant recipients. This may be a useful practice in settings where 24-hour estimation is not feasible or cumbersome, and where trends in proteinuria need to be monitored frequently.

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