

Comparison of urine protein creatinine ratio and 24 hours urine protein in detecting preeclampsia

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ABSTRACT

Aims: To assess the diagnostic accuracy of spot urine protein-creatinine ratio for detection of proteinuria in Preeclampsia.

Methods: Cross Sectional Descriptive Study was conducted in a total of 38 pregnant women in Paropakar Maternity and Women's Hospital in study period of 3 month. The correlation between protein-creatinine ratio in spot urine samples and urinary protein excretion in 24-hour collections were analyzed.

Results: Comparison of 24 hours urinary protein and protein-creatinine ratio in women with preeclampsia shows a significant correlation ($r=0.911$, $p<0.0001$). The cut-off protein-creatinine ratios which gave maximum area under the curve for 300mg protein for 24hrs was 0.27 (sensitivity: 94.6%, specificity: 100%, PPV: 100%, NPV: 33.3%); 2000 mg urine protein excretion was 2.1 (sensitivity and specificity of 100%); 3000mg protein excreted for 24hours was 3.0 (sensitivity: 83.3%, specificity: 92.3%, PPV: 83.3%, NPV: 93.3%. Area under the ROC for 24hours urine total protein of >300 mg, >2000 mg and >3000 mg/day were 0.946 (95%CI 0.873-1.019), 1 (95% CI 1.00-1.00) and 0.957 (95%CI 0.897- 1.016) respectively.

Conclusions: Spot urine protein-creatinine ratio is as accurate as to 24 hours urine protein determination of proteinuria in Preeclampsia.

Keywords: preeclampsia; proteinuria; protein-creatinine ratio.

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INTRODUCTION

Preeclampsia (PE) has a higher risk of maternal and neonatal mortality and morbidity. Early detection and management of patient with PE is therefore beneficial. Measurement of protein excretion in 24 hours urine collection has been considered gold standard for detecting proteinuria in PE. It is however impractical in outpatient setting, as it is cumbersome and time consuming test, delaying the diagnosis and management. Spot urine protein-creatinine ratio (PCR), a more rapid test if accurately predicts the result of 24hour urine would be valuable.

Clinical utility of urine PCR as a substitute of 24 hours urine protein excretion for detecting proteinuria in patient with preeclampsia is still unclear. Some studies show high correlation between spot urine

PCR and 24hours urine collection,¹⁻⁴ however some studies have conflicting results.⁵ Abnormal protein excretion is arbitrarily defined by 24-hour urinary excretion exceeding 300 mg; a urine P/C ratio ≥ 0.3 ; or persistent 30 mg/dl (1+ dipstick) protein in + random urine samples.⁶

This study aims to assess the diagnostic accuracy of spot urine compared to 24-hour urine protein for prediction of proteinuria in Preeclampsia.

METHODS

The study was conducted at Paropakar Maternity and Women's Hospital, Thapathali, Kathmandu from January 2018 to March 2018 with ethical approval. Among 4,857 obstetrics admission in three months, there were 84 cases of PE (1.7%) but only 38 were

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eligible by selection criteria. Patients from 19 to 41 years at 26 to 40 week of gestation were screened by dipstick followed by spot urine PCR and 24 hours urine protein for PE. Patient with pre-existing medical conditions like diabetes mellitus, renal disease, liver disease, thyroid disorder; pregnancy with UTI, pathological vaginal discharge, antepartum hemorrhage, twin pregnancy or women who delivered within urine collection day were excluded.

Spot mid-stream urine sample was taken prior to collection of 24hours urine sample. The urine PCR was determined on spot urine specimens. The concentration of both total protein and creatinine in urine was measured by a Spectrophotometry. Urinary microprotein was determined by dye binding method and creatinine by modified Jaffe method.

For 24 hour protein collection, the urine for detecting proteinuria was collected for 24 hours in a transparent jar with 5 liter capacity which was obtained from lab. Measurement of the 24-hour urine sample was performed on the same day as collections were completed.

The statistical analysis was done using SPSS version 16 statistical package. The quantitative variables like age, gestational age, were presented as mean and standard deviation. The qualitative variables i.e. parity and presence or absence of proteinuria (on both spot protein-creatinine ratio and 24 hours urinary proteins level) were presented by calculating frequency and percentages. Correlation between the two test was done by Pearson' correlation test, the p-value of <0.05 was considered significant. Receiver Operating Characteristic (ROC) analysis done by SPSS, and was used to determine sensitivity, specificity and likelihood ratios of urine PCR cutoff values to predict proteinuria.

RESULTS

Among 4,857 obstetrics admission during period of January 2018 to March 2018, there were 84 cases of PE (1.7%) but only 38 patients satisfied the selection criteria for the study. The median maternal age, body mass index (BMI) and gestational age were 25.2±5.5years (range20-40), 24.7±2.86 kg/m2 (range 20-33) and 32.8±3.8 weeks (range21-42) respectively; 86.8% were <36 weeks of gestation and 55.3% nulliparous [Table-1].

The mean protein level in 24 hour urine collection was 2.09 ± 1.57gm (range 0.24-4.81). The mean spot urine

PCR value was 1.97± 1.42 (range 0.22-4.90).There was a good positive statistical correlation between the spot PCR and 24-hour urine protein excretion, with a correlation coefficient(r) of 0.911(p<0.001) [Table-2 & Figure-1].

Table-1: Characteristics of preeclamptic population

Characteristics		Frequency (%)	Mean
Age (years)	<20	6 (15.8%)	25.2±5.5
	20-24	18 (47.4%)	
	25-29	7 (18.8%)	
	30-34	3 (7.9%)	
	35-39	3 (7.9%)	
	>40	1 (2.6%)	
Parity	Nulliparous	21 (55.3%)	-
	Multiparous	7 (44.7%)	
Gestational weeks	Extreme preterm (<28)	4 (10.5%)	32.8±3.8
	Preterm (28-36)	29 (76.3%)	
	Term (37-39)	5 (13.2%)	
	Postdated (40-42)	1 (2.6%)	
	Post term (>42)	0	
BMI (kg/m ²)	18.5-24.9	23 (60.5%)	24.7±2.86
	25-29.9	14 (36.8%)	
	30-34.9	1 (2.6%)	
	35-39.9	0	
	≥40	0	

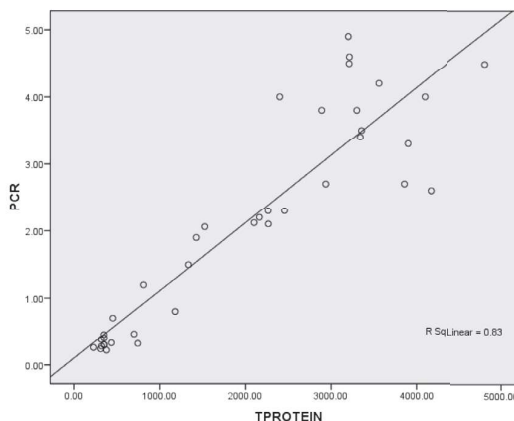


Figure-1: Correlation between PCR and 24 hour urine protein in PE

Table-2: Correlation between urine PCR and 24 hour urine protein in detecting PE

Protein Excretion	Range	Mean	r-value	p-value
24hour urine protein excretion (gm)	0.24-4.81	2.09 ± 1.57	0.911	<0.001
Spot Urine PCR	0.22-4.90	1.97± 1.42		

Among 38 patients of PE, 13 patients had BP range of 140-159/90-109mm of Hg, while 25 patients had BP of $\geq 160/110$ mm of Hg. On measuring proteinuria by spot urine PCR in patient with BP range 140-159/90-109 mm of Hg the range was between 0.24-3.5 whereas the mean was 1.49, which was comparable with 24 hours urine protein i.e. range of 0.31-3.9gm/24 hours and mean of 1.64. Similarly in case of BP $\geq 160/110$ the proteinuria detected by urine PCR had a range of 0.22-4.90 with the mean of 2.3 which was comparable to 24hours protein group i.e. range of 0.22-4.81gm/24hour and mean of 2.26/24hours. There was a strong correlation between urine PCR result and 24hours urine protein result in both group with $r=0.948$ and $r=0.908$ respectively [Figure-2].

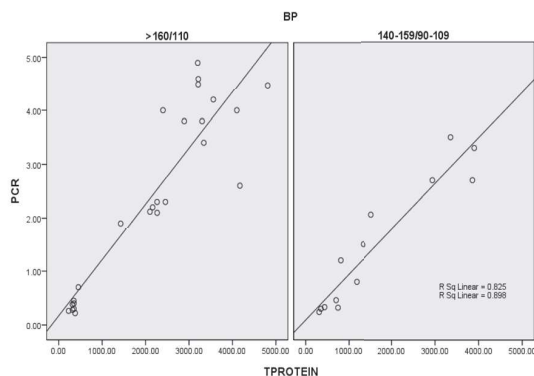


Figure-2: Correlation between PCR and 24 hr urine protein in relation to BP

Considering 24hours proteinuria as gold standard, the sensitivity, specificity, positive and negative predictive values were calculated. The best cut-off which gave the maximum area under curve was 0.27 for 300mg, 2.1 for 2000mg and 3.0 for 3000mg. A PCR above 0.27 predicts significant proteinuria for more than 300mg. (AUC 0.946, 95%CI:0.873-1.019) and sensitivity, specificity, PPV and NPV of 94.6%,

urine PCR of 2.1 predicts significant proteinuria (>2000 gm) with Sensitivity, Specificity, PPV and NPV all of 100%. Similarly, PCR ratio above 3.0 predicts significant proteinuria for more than 3000mg (AUC 0.957, 95%CI:0.897-1.016) and sensitivity, specificity, positive predictive value and negative predictive value of 92.3%, 83.3%, 92.3% and 83.3% respectively. There were 2 false positive and 2 false negative results. Accuracy of spot urine PCR on measuring urine protein >3000 mg was calculated to be 89% [Table-3].

Thus spot urine PCR excludes the presence of significant proteinuria and predicts severe proteinuria thus it can be used as an alternative to 24 hours total urine protein evaluation.

DISCUSSION

Clinical utility of urine PCR as a substitute of 24-hour urinary protein excretion has been validated in several studies in diabetic, nondiabetic nephropathies and some cases of PE.^{1-5,7-10}, Demirci O et al¹⁰, Kayatas S et al³, Bansal B et al⁴, Shahbazian et al¹, Wheeler II TL et al² and Robert M et al¹¹ found a significant correlation between 24hrs protein excretion and urine PCR with $r=0.758, 0.828, 0.83, 0.84, 0.88, 0.94$ ($p<0.0001$) however study by Durnwald C shows poor correlation between spot urine PCR and 24 hour urine protein with $r=0.45$.⁵ This study shows a good correlation between urine PCR and 24hour urine protein with $r=0.83$ and $p<0.001$.

Although studies have shown good correlation between PCR and 24 hour urine protein estimation in PE there is no reliable evidence about the optimal cut-off value for spot PCR for defining PE. In studies by Kayatas S et al³, Shahbazian N et al¹, Khan SM et al¹²

Table-3: Test performance of spot P/C ratio assessment for 24hr urine protein result

24 hrs urine protein (mg)	AUC	Optimal spot P/C ratio (mg/mg)	Sensitivity	Specificity	PPV	NPV
>300	0.946	0.27	94.6%	100%	100%	33.3%
>2000	1	2.1	100%	100%	100%	100%
>3000	0.957	3.00	92.3%	83.3%	92.3%	83.3%

100%, 100% and 33.3% respectively). There were 2 false negative values but no false positive values. On calculating accuracy Spot urine PCR was 94.4% accurate as 24 hour urine protein in measuring urine protein excretion >300 mg in preeclampsia. The

and Demirci O et al¹⁰ the cut of values for detecting PE was 0.28, 0.20, 0.3 and 0.45. Similarly this study shows a good correlation between spot urine PCR and 24 hour urine protein in detection of PE ($r^2=0.84$). Despite the high degree of linear correlation, the best cutoff for detecting significant proteinuria

couldn't be described. For urine protein excretion of 300mg cutoff value in this study was 0.27. It is a very good test for discriminating between significant and insignificant proteinuria as demonstrated by an area under the ROC curve of 0.94. The cutoff value on ROC analysis which signified proteinuria was 0.27, which gave sensitivity of 94.6% and Specificity of 100%. However the NPV is very low i.e. 33.3%. Increasing sensitivity, the best cutoff point obtained, rules out the potential consequences of missing the diagnosis of preeclampsia. If falsely negative, clinicians may fail to intervene patients who actually have preeclampsia increasing rate of mortality and morbidity. Alternatively, a false positive PCR leads to unnecessary intervention to the patients and possible iatrogenic prematurity. A cutoff below 0.23 ruled out significant proteinuria; however the specificity was 0%. Thus to maximize the specificity while maintaining a sensitivity of $\geq 90\%$, we set our criterion of positivity as >0.27 . This yielded a sensitivity of 94.6% and a specificity of 100% the negative predictive value was 33.3% in our population. However, present study could not determine a definite cutoff point for detection of significant proteinuria. The best cutoff value of >0.27 that yielded by ROC analysis had a high specificity (100%) and sensitivity (94.6%) but low NPV. In Rodriguez et al¹³ study, most of the false negative and false positive test results were within 50 mg of the cutoff point of 300 mg for a 24-hours urine, which is similar to our study, the false negative test were within 80mg of the cutoff point for 300mg. While in study by Taherian et al⁶, false negative results ranged from 300 to 1100 mg (mean value of 518 mg). However for patients with a high pretest probability of disease and a negative random urinary PCR, repeating the test or proceeding with collection of a 24-hours urine is a reasonable option. Repeating a random sample is much easier and quicker to accomplish it.^{6,13}

We were also able to assess the usefulness of the random urine PCR for the diagnosis of severe proteinuria ($>2000\text{mg}$) in our data set. The area

under the ROC curve for PCR at $>2000\text{mg}$ of protein excretion in 24 hour protein excretion is 1.00 (95% confidence interval 1.00 and 1.00). The cutoff value of >2.1 yields a sensitivity of 100% and a specificity of 100% in detecting proteinuria $>2000\text{gm}$. Similarly Wheeler et al.⁵ reported that PCR was 100% sensitive and specific to detect the proteinuria $>5\text{ g/day}$ in preeclamptic women. Also for random urine PCR for the diagnosis of severe proteinuria ($>3000\text{mg}$) in our data set, the area under the ROC curve for PCR at $>3000\text{mg}$ of protein excretion in 24 hour protein excretion is 0.957 (95% CI: 0.897 and 1.016). The cutoff value of > 3 yields a sensitivity of 83.3% and a specificity of 92.3% in detecting proteinuria $>3000\text{gm}$.

In this study there was no difference between the patients with proteinuria in terms of age, gestational age or BMI. Furthermore our study excluded patients with chronic hypertension, diabetes and renal disease, in whom preexisting proteinuria was always likely. Limitation of this study was the sample size which was very less. Similarly our study population was hospitalized and non ambulatory, thus there is a question whether this can be applied to ambulatory patients. The samples were obtained before the 24-hours urine collection, thus decreases the potential for a falsely elevated PCR after the completion of the 24-hours urine collection as disease being progressive in nature. It however avoided the potential impact of prolonged bed rest before sampling on the PCR.

CONCLUSIONS

Spot urine protein-creatinine ratio which has a strong correlation ($r=0.911$) with 24 hours urine protein analysis can be an option for detecting proteinuria. The test is as accurate as 24 hour urine protein to detect preeclampsia by urine protein $>300\text{mg}$ (Sensitivity-94.6%, Specificity-100%, PPV-100% and NPV-33.3%) and predict severe preeclampsia by urine protein $>2000\text{mg}$ (sensitivity and specificity of 100%) and $>3000\text{gm}$ (Sensitivity-83.3%, Specificity-93.3%, PPV-83.3%, NPV-92.3%).

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