24 HOURS URINARY PROTEIN VERSUS SPOT PROTEIN-CREATININE FOR ASSESSING PROTEINURIA IN PRE-ECLAMPSIA- A COMPARATIVE STUDY

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ABSTRACT

BACKGROUND

The objective of this study is to study the relationship between the 24-hour urinary protein and random urinary spot protein creatinine ratio in pre-eclampsia. This study also aims to determine the ability of random spot protein-creatinine ratio for prediction of significant proteinuria.

MATERIALS AND METHODS

This was a cross-sectional study conducted on 100 antenatal cases of pre-eclampsia with urinary dipstick value $\geq 1+$; 24-hour urinary sample and a next morning random sample for urinary PCR were collected from all the patients. Amount of proteinuria was estimated by turbidimetric method using sulphosalicylic acid and urinary creatinine was calculated by Jaffe's method; 24-hour urinary protein ≥ 300 mg/24 hours or urinary Protein-Creatinine Ratio ≥ 0.3 is taken as significant proteinuria. The data thus collected were analysed using appropriate statistical methods.

RESULTS

61% were primi, 39% were multiparous. Among multiparous, 43.6% of patients were positive for previous history of pre-eclampsia. All of them had significant urinary PCR. On comparing the 24-hour urinary protein with urinary protein-creatinine ratio, the sensitivity and specificity of urinary PCR is 100% and 95%, respectively. The positive and negative predictive value is 98.77% and 100%, respectively. The diagnostic accuracy is 99%. Measure of agreement tests McNemar test = 1.000, Kappa statistics $p = 0.968$ show perfect agreement. Youden Index and Area under the ROC Curve = 1, which implies 100% accuracy for PCR significant group with respect to 24-hour urinary protein. From our study, random urinary spot protein-creatinine ratio has a significant linear correlation with 24-hour urinary protein in pre-eclampsia. Since the measure of agreement between these two is perfect, urinary spot protein-creatinine ratio can be used as an excellent alternative for the time consuming 24-hour urinary protein estimation in patients with pre-eclampsia.

CONCLUSION

Spot protein-creatinine ratio provided a very useful, simple and convenient method for quantitative assessment of proteinuria in pre-eclamptic patients and can replace 24-hour urine collection method in indoor, outpatients and in follow-up clinics as it gives quick and reliable results and avoids the inconvenience and short comings associated with 24-hour urine collection. This study also proves that urinary dipstick alone has a poor sensitivity and specificity in diagnosing proteinuria of pre-eclampsia.

KEYWORDS

Urine Dipstick, Protein-Creatinine Ratio, 24 Hours Urinary Protein and Pre-eclampsia.

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BACKGROUND

Hypertensive disorder of pregnancy complicates approximately 15 - 20% of pregnancies of which pre-eclampsia occurs in 2 - 8%. Pre-eclampsia accounts for 15 - 20% of maternal mortality and a high amount of maternal morbidity.

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It is a major pregnancy complication causing preterm birth which is often iatrogenic, intrauterine growth restriction, abruption and intrauterine foetal demise which contribute significantly to perinatal mortality and morbidity.

Estimation of proteinuria is essential for making diagnosis, to assess the severity of disease and also for predicting foetomaternal outcome in pre-eclamptic pregnancies. For estimating the amount of protein in urine collection of 24 hours, urinary sample is taken as gold standard, but it is time consuming, cumbersome and inconvenient.

Routine simple dipstick urine analysis has low sensitivity, high false positive and false negative results. Also, its results are being influenced by maternal hydration status, diurnal variation, presence of infection, exercise, etc.

So, we can use random urinary spot protein-creatinine ratio instead of 24-hour urinary protein to detect significant proteinuria. In this method, urinary protein concentration is

divided by GFR independent of urinary creatinine concentration. Therefore, it is a useful reference.

MATERIALS AND METHODS

Study Period

One year at Institute of Obstetrics and Gynaecology, Egmore, Chennai.

Study Design

Prospective Study.

In this study, 100 admitted antenatal cases of pre-eclampsia with urinary dipstick value $\geq 1+$ were selected. General physical and obstetric examination was done for all; 24 hours urinary sample and a next morning random sample for urinary PCR were collected from all the patients. Amount of proteinuria was estimated by turbidimetric method using sulphosalicylic acid and urinary creatinine was calculated by Jaffe's method; 24-hour urinary protein ≥ 300 mg/24-hour or urinary Protein-Creatinine ratio ≥ 0.3 is taken as significant proteinuria.

The Tests were carried out as follows

The patients were instructed to collect the 24-hour urine starting from the second urine sample in the morning till the first urine sample next day morning. A sample was collected on the next day for spot protein/creatinine ratio estimation. Amount of proteinuria is estimated by using turbidimetric (Sulphosalicylic acid) method. The results for protein excretion is negative if the 24-hour urinary protein is < 300 mg/24 hours, protein-creatinine ratio < 0.3 , clinically significant proteinuria if urinary protein is ≥ 300 mg/24 hours and protein-creatinine ratio ≥ 0.3 .

The ISSHP (International Society for the Study of Hypertension in Pregnancy) defined significant proteinuria as,

1. 24-hour urinary protein ≥ 300 mg/day.
2. Random protein creatinine ratio ≥ 30 mg/mmol.

The data thus collected were analysed using appropriate statistical methods.

Inclusion Criteria

This study will be carried out on 100 randomly selected, admitted antenatal cases with pre-eclampsia of more than 20 weeks gestation.

Exclusion Criteria

1. Urinary tract infection.
2. Preexisting renal or vascular disease.
3. Chronic hypertension.
4. Diabetes mellitus.

ANALYSIS AND RESULTS

Among 100 study patients, 80 had significant proteinuria; 66% of the patients were in the age group of 20 to 30 years, among them 87.9% were significant for urinary PCR.

61% were primi, 39% were multiparous. Among multiparous 43.6% of patients were positive for previous history of pre-eclampsia. All of them had significant urinary PCR.

The sensitivity and positive predictive value of dipstick is 67.5% (95% CI, 56.64 - 76.76) and 72.97% (95% CI, 61.91 - 81.77) respectively. The diagnostic accuracy is 54% with respect to 24-hour urinary protein.

The sensitivity and positive predictive value of urinary dipstick is 67.9% (95% CI, 57.12 - 77.06) and 74.32% (95% CI, 63.35 - 82.9) respectively. The diagnostic accuracy is 55% with respect to urinary PCR.

On comparing the 24-hour urinary protein with urinary protein-creatinine ratio, the sensitivity and specificity of urinary PCR is 100% and 95% respectively. The positive and negative predictive value is 98.77% and 100% respectively. The diagnostic accuracy is 99%.

Measure of agreement tests McNemar test = 1.000, Kappa statistics $p = 0.968$ show perfect agreement. Coefficient of determination (r^2) is 0.9571, which infers a very good correlation between 24-hour urinary protein and urinary spot protein-creatinine ratio.

Youden Index and Area under the ROC Curve = 1, which implies 100% accuracy for PCR significant group with respect to 24-hour urinary protein. In the ROC Curve, the value of 0.3 has maximum sensitivity and specificity.

Crosstab					
			24-Hour Urinary Protein Significance		
			0	1	Total
Urinary PCR Significance	0	Count	19	0	19
		% of Total	19.0%	.0%	19.0%
	1	Count	1	80	81
		% of Total	1.0%	80.0%	81.0%
	Total	Count	20	80	100
		% of Total	20.0%	80.0%	100.0%

Table 1. Urinary PCR Significance
***24-Hour Urinary Protein Significance**

McNemar $p = 1.0000$

Kappa Statistics = 0.968

Chi-Square Tests		
McNemar Test	Value	Exact Sig. (2-Sided)
N of Valid Cases	100	1.000a

Table 2

Binomial distribution used.

Symmetric Measures				
Measure of Agreement	Value	Asymp. Std. Error ^a	Approx. T ^b	Approx. Sig.
Kappa	.968	.032	9.686	.000
N. of Valid Cases	100			

Table 3

- Not assuming the null hypothesis.
- Using the asymptotic standard error assuming the null hypothesis.

Graph 1. Bar Chart shows the Relationship between Urinary Dipstick and PCR

Graph 2. The Bar Chart shows the Relation between Urinary PCR and 24-Hour Urinary Protein

Graph 3. Shows Linear Relationship between 24-Hour Urinary Protein and Spot Urinary Protein-Creatinine Ratio

Correlation

Variable Y	Urinary Protein
Variable X	Urinary PCR

Table 4

Sample Size	100
Correlation coefficient r	0.9783
Significance level	P < 0.0001
95% Confidence interval for r	0.9679 to 0.9854

Table 5

Graph 4

ROC Curve

Variable	Urinary PCR
Classification Variable	hr_urinary_protein_significance

Table 6

Sample Size		100
Positive Group	hr_urinary_protein_significance = 1	80
Negative Group	hr_urinary_protein_significance = 0	20

Table 7

DISCUSSION

Testing for proteinuria is very important in the treatment of pre-eclampsia.¹ The gold standard testing detection of proteinuria, 24-hour protein collection, is not always performed correctly and can cause delayed diagnosis and the application of treatment. Due to high accuracy, reproducibility and convenience compared with 24-hour protein collection, the P/C ratio in spot urine was developed as an alternative test in the pregnant population.⁽²⁾ Morales et al⁽³⁾ reported the potential error in determining protein in a spot urine sample due to daily variation that does not exceed the error in collecting a 24-hour urine sample. Also, until now, the majority of studies evaluating spot urine P/C ratio in pregnant women with suspected pre-eclampsia have been found to be closely correlated with the 24-hour urine protein measurement.⁽⁴⁻⁹⁾ However, in pregnant women, there is no reliable evidence about the optimal cut-off value for spot urine P/C ratio for defining pre-eclampsia. The most recent meta-analysis⁽¹⁰⁾ implied that the optimum threshold for P/C ratio to define significant proteinuria is between 0.30 and 0.35 regarding sensitivity and specificity values above 75%; when the sensitivity and specificity above 80% was accepted, there was

no cut-off found.⁽¹⁰⁾ We found that P/C ratio is more sensitive and more specific for the detection of proteinuria > 1 g/day. From our study, we concluded that random urinary spot protein-creatinine ratio has a significant linear correlation with 24-hour urinary protein in pre-eclampsia. Since the measure of agreement between these two is perfect urinary spot protein-creatinine ratio can be used as an excellent alternative for the time consuming 24-hour urinary protein estimation in patients with pre-eclampsia. Also urinary dipstick alone has a poor sensitivity and specificity in diagnosing proteinuria of pre-eclampsia.

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