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Original Research Article

Comparative evaluation of different methods to quantify proteinuria in preeclampsia

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ABSTRACT

Background: Worsening of condition in preeclampsia is indicated by progressive proteinuria, hence its quantification helps in decision making and plan treatment accordingly. The present study was undertaken to compare different methods of estimation of proteinuria to find best method for quantification.
Methods: It was a hospital based prospective study conducted on a group of 100 pregnant women diagnosed as preeclampsia after 20 weeks of gestation, they were subjected to different methods of quantification of proteinuria after admission in department of obstetrics and gynaecology, Narayana medical college and hospital, Nellore over a period of one year.
Results: Present study showed strong positive strength of association of SSA test was higher compared to the spot urinary PCR and spot urinary dipstick. To assess the predictability of three methods compared against 24-hour urine protein estimation by ROC curve. The AUC of the SSA test and spot urinary PCR was stronger than the urinary dipstick. Study showed a significant better method as SSA>>Urinary PCR>>dipstick with accuracy of 96.04%, 95.0% and 54% respectively.
Conclusions: This study concluded that spot urine SSA and urine PCR are reliable investigations compared to dipstick method. So, spot urine SSA and urine PCR can be used for detection of proteinuria in pregnant women with pre-eclampsia with high accuracy, which is more rapid than time consuming 24-hour urine protein estimation. Thus, this quick method with high accuracy is very useful to prevent feto-maternal morbidity and mortality in India.

Keywords: Dip stick test, Preeclampsia, Proteinuria, Sulphosalicylic acid (SSA), Urine protein-creatinine ratio (PCR)

INTRODUCTION

Among hypertensive disorders of pregnancy preeclampsia is the leading cause and complicates 5%–10% of pregnancy.[1] It was defined as a multisystemic disorder characterized by new onset of hypertension [i.e. systolic blood pressure (SBP) ≥140 mmHg and/or diastolic blood pressure (DBP) ≥90 mmHg] and proteinuria (>300 mg/24 hours) arising after 20 weeks of gestation in a previously normotensive woman.[1] Recently, the definition of Preeclampsia has been widened. It is defined as gestational hypertension accompanied by ≥1 new-onset conditions at or after 20 weeks of gestation which include:

Proteinuria (≥30 mg/mol protein: creatinine ratio, ≥300 mg/24 hour, or ≥2 + dipstick), Maternal organ dysfunction which includes, acute kidney injury, liver involvement with or without right upper quadrant or epigastric pain, neurological complications or haematological complications, Uteroplacental dysfunction.[2]

Pre-eclampsia thought to arise from imbalance between foetal demands and uteroplacental supply. Basic pathology is endothelial dysfunction and vasospasm of small blood vessels of all organ systems, particularly those in kidney, uterus, placenta and brain.[3] Proteinuria is one of the essential criteria to monitor severity of disease and predict complications. In pre-eclampsia, renal perfusion and

glomerular filtration rate are reduced. Preeclampsia appears to produce a characteristic change in the kidneys termed as glomerular capillary endotheliosis.[4] In non-pregnant women minimal quantity of proteins (up to 150 mg/day) are excreted in urine, due to renal changes during pregnancy, proteinuria in excess of 300 mg/day is considered as abnormal. Methods for quantification of proteinuria vary, the 24-hour urine protein excretion method is cumbersome and is time-consuming, it may give inaccurate results because of improper collection. There are two rapid methods for quantitative estimation of proteinuria-spot urinary protein: creatinine ratio (UPCR) and dipstick method.[5,6] This study was undertaken to compare different estimation methods of proteinuria like sulphosalicylic acid test, dip stick test, spot urine protein-to -creatinine ratio and 24-hour urine protein in preeclampsia to find best method of quantification.

Aim

The aim was to compare different methods to quantify and estimate proteinuria in preeclampsia women and to find out best method for proteinuria estimation.

Objectives

Estimation of proteinuria by sulphosalicylic acid test, dip stick test, spot urine protein-to-creatinine ratio in preeclampsia women and to compare the methods to identify the best method for proteinuria estimation among the women with preeclampsia.

METHODS

It was a hospital based prospective study conducted on a group of 100 pregnant women who have been diagnosed as preeclampsia after 20 weeks of gestation, each of these pregnant women were subjected to different methods of quantification of proteinuria after admission in antenatal ward in department of obstetrics and gynaecology, Narayana medical college and hospital, Nellore over a period of one year (August 2021-August 2022).

Inclusion criteria

Pregnant women more than 20 weeks of gestation with hypertension of 140/90 mmHg or higher on two occasions, 4 hours apart associated with proteinuria.

Exclusion criteria

Patients with renal disease, diabetes, urinary tract infections, pre-existing hypertension, chronic hypertension.

The study comprised of pregnant women who are more than 20 weeks of gestation diagnosed as preeclampsia fulfilling the inclusion and exclusion criteria. Written and informed consent was taken from all pregnant women participating in the study.

The pregnant women in the study were subjected to a detailed history and general abdominal and pelvic examination. A first voided morning urine sample was obtained for sulphosalicylic acid test, dipstick test, spot urine protein creatinine ratio.

Subsequent urine samples were collected for 24 hours, including a next-day first-morning voided sample for the 24-hour urine protein estimation. Sulphosalicyclic acid test was done by standard methods, dipstick test with kits. Spot urine protein estimation was performed by the colorimetric method. Spot urine creatinine estimation was performed by the modified Jaffe's method using a standard autoanalyzer and spot urine protein to spot urine creatinine ratio was calculated and 24-hour urine protein was estimated.

All the collected data was analysed using SPSS v21 operating on windows 10. The demographic data and study variables were summarised as mean, standard deviation, frequency and percentage. The summarized data were represented using tables, figures. Chi square test was used and the strength of association between the variables were analysed using Pearson's correlation. The ROC was done to assess the diagnostic accuracy of the method. A p value of <0.05 was considered statistically significant.

RESULTS

A total of 100 pregnant women with pre-eclampsia were included in study after obtaining the informed consent.

Table 1: The mean age of pregnant mothers included in the study.

	N	Minimum	Maximum	Mean	SD
Age in years	100	17	39	25.47	5.58

The mean age of patients was found to be 25.47±5.58 years (Table 1).

Table 2: Age wise distribution of participants in the study.

Age wise group	Frequency	Percent
18-20 years	19	19.0
21-25 years	38	38.0
26-30 years	23	23.0
31-40 years	20	20.0

Table 3: Distribution of gravida among study participants.

		Frequency	Percentage
Gravida	1	64	64
	2	30	30
	3	6	6

Table 4: Comparison of the result by urinary dipstick and urinary PCR with urinary 24-hour protein estimation by chi-square test.

24-hour urinary protein significance						Chi square (p value)
		<300 mg		>300 mg		
		Count	Column N%	Count	Column N%	
Spot urinary dipstick	Absent	1	4.5	25	32.1	6.74 (0.001)**
Spot urinary PCR	Present	21	95.5	53	67.9	72.32 (0.001)**
	<0.3	18	81.8	1	1.3	
Spot sulphosalicylic acid test	>0.3	4	18.2	77	98.7	84.615 (0.001)**
	<30 mg/dl	21	95.5	3	3.8	
	>30 mg/dl	1	4.5	75	96.2	

**P value- significant

Majority of participants were in age group of 21-25 years (38%) followed with 23% in age of 26-30 years, 20% in 31-40 years and 19% in 18-20 years of age (Table 2).

Among the patients, majority were primigravida (64%) (Table 3).

The strength of association of sulphosalicyclic acid test was r=0.999, p<0.05, urinary spot protein creatinine ratio was r=0.976, p<0.05 and for spot urinary dipstick was r=0.896, p<0.05 (Tables 4 and 5). Study showed a significant better method as sulphosalicyclic acid test >>urinary spot protein creatinine ratio >>dipstick respectively.

Table 5: Correlation of the result by urinary dipstick and urinary PCR with urinary 24-hour protein estimation by Pearson's correlation.

		24-hour urinary protein
Spot urinary dipstick	r	0.896**
Spot urinary PCR	r	0.976**
Spot sulphosalicylic acid test	r	0.999**

**r value- strong positive strength of association.

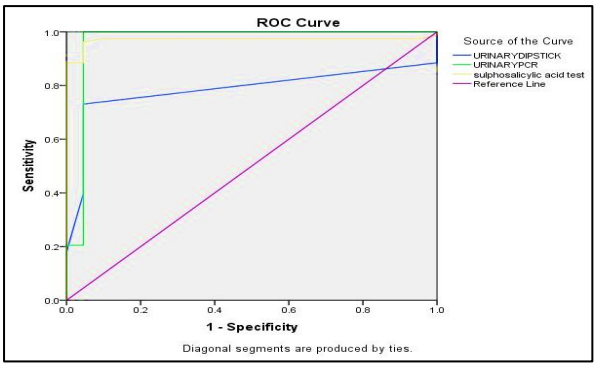

Figure 1: ROC curve in predicting the significant proteinuria using different test method.

The AUC of the Sulphosalicyclic acid test and spot urinary protein creatinine ratio was stronger than the urinary Dipstick method in correlation with 24hr urinary total protein estimation method.

On assessment of the ROC curve (Figure 1) to assess the predictability of three methods for spot urine compared against 24-hour urine protein estimation, the AUC for the sulphosalicylic acid was significantly better (AUC=0.970, p<0.05) compared to the Spot urinary protein creatinine ratio (AUC=0.964, p<0.05) and for urinary dipstick (AUC=0.784, p<0.05) (Table 6).

Table 6: The AUC on ROC in predicting the significant proteinuria using different test method.

Test Result Variable(s)	Area	Asymptotic Sig.[b]	Asymptotic 95% CI	
			Lower Bound	Upper Bound
Urinary dipstick	0.784	0.001	0.692	0.877
Urinary PCR	0.964	0.001	0.894	1.000
Sulphosalicylic acid	0.970	0.001	0.935	1.000

The AUC of the sulphosalicyclic acid test and spot urinary protein creatinine ratio was stronger than the urinary Dipstick method in correlation with 24-hour urinary total protein estimation method.

Table 7: The diagnostic characteristics of urinary dipstick method.

Spot urinary dipstick	Value	95% CI
Sensitivity	67.95%	56.42-78.07%
Specificity	4.55%	0.12-22.84%
Positive predictive value	71.62%	67.88-75.09%
Negative predictive value	3.85%	0.57-21.81%
Accuracy	54.00%	43.74-64.02%

On assessment of diagnostic accuracy spot urinary dipstick method showed sensitivity of 67.95%, specificity of 4.55%, PPV of 71.62%, NPV of 3.85% and overall accuracy of 54% (Table 7).

Spot urinary PCR documented a sensitivity of 98.72%, specificity of 81.82%, PPV of 85.06%, NPV of 94.74% and overall accuracy of 95.0% (Table 8).

Table 8: The diagnostic characteristics of urinary protein creatinine ratio method.

Spot urinary protein-creatinine ratio	Value	95% CI
Sensitivity	98.72%	93.06-99.97%
Specificity	81.82%	59.72-94.81%
Positive predictive value	95.06%	88.80-97.90%
Negative predictive value	94.74%	71.77-99.22%
Accuracy	95.00%	88.72-98.36%

Spot SSA recorded a sensitivity of 99.15%, specificity of 95.65%, PPV of 98.68%, NPV of 88% and overall accuracy of 96.04% (Table 9).

Table 9: The diagnostic characteristics of spot urinary Sulphosalicylic acid method.

Sulphosalicylic acid test	Value	95% CI
Sensitivity	99.15%	89.17-99.20%
Specificity	95.65%	78.05-99.89%
Positive predictive value	98.68%	91.68-99.80%
Negative predictive value	88.00%	70.67-95.71%
Accuracy	96.04%	90.17-98.91%

Study showed a significant better method as sulphosalicyclic acid test >>urinary spot protein creatinine ratio >>dipstick with accuracy of 96.04%, 95.0% and 54% respectively.

DISCUSSION

Early identification of preeclampsia reduces the cost of antenatal care by identifying the women who are at high risk thus leading to improvement in management of hypertensive disorders at later weeks. Urine routine is one of the most important examinations during antenatal check-ups.

We aimed to compare different methods to quantify and estimate proteinuria in pre-eclampsia women and to find the best method for proteinuria estimation.

A total of 100 pregnant women with pre-eclampsia were included after obtaining the informed consent. General, physical and obstetric examination was done for all.

24-hour urinary sample and a next morning random sample for dipstick, sulphosalicylic acid, urinary PCR was collected from all patients.

The mean age of patient was found to be 25.47±5.58 years. Majority of participants were in age group of 21-25 years (38%) followed with 23% in age of 26-30 years, 20% in 31-40 years and 19% in 18-20 years of age. Among them majority were primigravida.

In similar to present study, Amin et al found the mean age of patients was 27.4±4.3 years with minimum of 20 years and maximum of 41 years of age, and 51% women were primipara.[5]

Similar to present study Sharma et al documented majority were in the age group of 21-30 years of age (87.92%), followed with 7.9% in 31-40 years and 7.14% less than 20 years of age.[7]

On correlation of the various estimations of spot urine protein with 24-hour urinary total protein, we found a significant positive strength of association between them. The strong positive strength of association of sulphosalicylic acid test was higher compared to the spot urinary PCR and spot urinary dipstick result.

All the 3 methods of spot urine were strongly correlated with the sulphosalicyclic acid test being superior followed with spot urine protein creatinine ratio and dipstick method.

In study by Archana et al showed a significant strong correlation of spot UPCR with 24-hour urinary proteinuria with r=0.88.[6]

On assessment of the ROC curve to assess the predictability of three methods for spot urine compared against the 24hr urine protein estimation, The AUC of the SSA and urinary PCR was stronger than the urinary Dipstick method in correlation with 24-hour urinary total protein estimation method.

In study by Berthet et al, the area under the curve for spot PCR was 0.92, with higher accuracy in diagnosing the proteinuria and thus pre-eclampsia.[11]

In a study, Sharma et al documented the AUC for PCR was 0.793, $p<0.05$.[7]

On assessment of diagnostic accuracy in term of sensitivity, specificity, PPV, NPV and accuracy of each method compared with the 24-hour urinary total protein estimation.

Spot urinary dipstick method showed the sensitivity of 67.95%, specificity of 4.55%, PPV of 71.62%, NPV of 3.85% and overall accuracy of 54%.

On assessment for spot urinary PCR we documented a sensitivity of 98.72%, specificity of 81.82%, PPV of 85.06%, NPV of 94.74% and overall accuracy of 95.0%.

Similarly, on assessment for spot SSA we recorded a sensitivity of 99.15%, specificity of 95.65%, PPV of 98.68%, NPV of 88% and overall accuracy of 96.04%.

Study showed a significant better method as sulphosalicyclic acid test >>urinary spot protein creatinine ratio >>dipstick with accuracy of 96.04%, 95.0% and 54% respectively.

In study by Amin et al, dipstick method showed 59% sensitivity and 67% specificity for prediction of significant proteinuria. Area under curve for UPCR was 0.89 showing 82% sensitivity, specificity of 90% and 12.5% false positive rate for cut off value of 0.45.[5]

In study by Sharma et al, the optimal spot P/C ratio cut off point was 0.2 for 300 mg/24 hours of protein excretion, with a sensitivity, specificity, positive predictive value and negative predictive value of 91.2%, 87.8%, 94.4% and 96.8% respectively.[7]

Adequacy of 24-hour collection was not uniformly reported, sample size was limited to 100 as study requires admission for 24-hour collection. cut off values for urine protein:creatinine ratio differs because of variation in laboratory methods used to estimate urine protein and creatinine levels.

CONCLUSION

This study concluded that spot urine SSA and urine PCR are reliable investigations compared to dipstick method. So, spot urine SSA and urine PCR can be used for detection of proteinuria in pregnant women with pre-eclampsia with high accuracy, which is more rapid than time consuming 24-hour urine protein estimation. Thus, this quick method with high accuracy is very useful to prevent feto-maternal morbidity and mortality in India.

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