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Original Research Article

"A SYUDY ON COMPARATIVE EVALUATION OF FOUR DIFFERENT METHODS TO QUANTIFY PROTEINURIA IN PRE-ECLAMPSIA IN A TERTIARY CARE HOSPITAL"

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ABSTRACT:

Background: Preeclampsia is a progressive, multisystem disorder due to spasm of small blood vessels of all organ systems characterized by new-onset hypertension and end- organ dysfunction in the last half of pregnancy.

OBJECTIVES:

• Estimation of proteinuria by sulphosalicylic acid test in women with preeclampsia.

• Estimation of proteinuria by dip stick test in women with preeclampsia.

• Estimation of proteinuria by spot urine protein - to -creatinine ratio in preeclampsia women.

• Compare the methods to identify the best method for proteinuria estimation among the women with preeclampsia.

Material & Methods: Study Design: Prospective hospital based clinical study. **Study area:** Study conducted in the Department of Obstetrics and Gynaecology, Murshidabad Medical college, Berhampore, Murshidabad, West Bengal. **Study Period:** Sep. 2021 - Aug. 2022. **Study population:** Pregnant women after 20weeks of gestation diagnosed as preeclampsia and admitted in antenatal ward in obstetrics and gynaecology department, Murshidabad Medical college, Berhampore, Murshidabad, West Bengal. **Sample size**: Study consisted a total of 100 subjects. **Sampling Technique:** Simple Random sampling method. **Study tools and Data collection procedure:** The pregnant women diagnosed as preeclampsia meeting the inclusion and exclusion criteria included in the study. 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 PCR. Subsequent urine samples were collected for 24 h, including a next-day first-morning voided sample for the 24-h urine protein estimation.

Results: 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 for the

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Sulphosalicylic acid was found to be significantly better (AUC=0.970, p<0.05) compared to the urinary PCR (AUC=0.964, p<0.05) and for urinary dipstick it was AUC=0.784, p<0.05.
CONCLUSION: This study concluded that spot urine sulphosalicylic acid and urine protein-creatinine ratio are reliable investigations compared to the dipstick method to assess the proteinuria in hypertensive pregnant women or for diagnosis of pre-eclampsia. So, spot urine Sulphosalicylic acid and urine protein-creatinine ratio can be used for detection of proteinuria in pregnant women with suspected pre-eclampsia with high accuracy, which is more rapid than time consuming 24-hour urine protein estimation.
Keywords: Preeclampsia, urine sulphosalicylic acid, urine protein-creatinine ratio

INTRODUCTION:

Preeclampsia is a progressive, multisystem disorder due to spasm of small blood vessels of all organ systems characterized by new-onset hypertension and end- organ dysfunction in the last half of pregnancy. Hypertensive disorders complicate up to 5-10% of pregnancies. Of which preeclampsia occurs in 3.9%. It remains as leading cause of both direct maternal and perinatal mortality. 16% of maternal deaths attributed to hypertensive disorders in pregnancy.[1,2]

It is said that, pre-eclampsia and eclampsia contributes to death of a woman every 3 minutes worldwide. Primary prevention of pre-eclampsia is not possible, as the exact cause remains unclear. Secondary prevention, to identify the pregnant women who are at risk of developing gestational hypertension, in order to avoid dangerous and life threatening complications was the aim of various researchers and this led to the interest in screening.

Screening is the deliberate examination of substantial segments of population in search for a disease at its earlier stage, interfere at optimum time and improve outcome is a logical extension of the role of preventive medicine. For a screening test to be of value, it should be selective, easy to perform and reliably cheap. It should increase predictive value and prophylactic measures must be effective.

In India prevalence of preeclampsia ranges from 8-10% contributing to maternal and perinatal morbidity and mortality. [3]

In pre-eclampsia, renal perfusion and glomerular filtration are reduced. Pre- eclampsia appears to produce a characteristic changes in the kidneys termed as glomerular capillary endotheliosis. Proteinuria is a major indicator of pre- eclampsia and one of diagnostic criteria of its severity. Estimation of proteinuria is essential not only for making the diagnosis and also for predicting maternal and fetal outcome.[4]

Hence The present study was undertaken to compare different estimation methods of proteinuria like sulphosalicylic acid test, dip stick test, spot urine protein- to -creatinine ratio and 24hr urine protein in preeclampsia to find best method of quantification.

OBJECTIVES:

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

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Material & Methods:

Study Design: Prospective hospital based clinical study.

Study area: Study conducted in the Department of Obstetrics and Gynaecology, Murshidabad Medical college, Berhampore, Murshidabad, West Bengal.

Study Period: Sep. 2021 - Aug. 2022.

Study population: Pregnant women after 20weeks of gestation diagnosed as preeclampsia and admitted in antenatal ward in obstetrics and gynaecology department, Murshidabad Medical college, Berhampore, Murshidabad, West Bengal.

Sample size: Study consisted a total of 100 subjects.

Sampling Technique: Simple Random sampling method.

Inclusion Criteria:

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

Exclusion criteria:

• Renal disease
• Diabetes
• Urinary tract infection
• Pre-existing hypertension
• Chronic hypertension

Ethical consideration: Institutional Ethical committee permission was taken prior to the commencement of the study.

Study tools and Data collection procedure:

The pregnant women diagnosed as preeclampsia meeting the inclusion and exclusion criteria included in the study. 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 PCR. Subsequent urine samples were collected for 24 h, including a next-day first-morning voided sample for the 24-h 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 autoanalyser and spot urine protein to spot urine creatinine ratio was calculated and 24 hr urine protein was estimated.

Statistical analysis:

All the collected data was entered in excel sheet and 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, bar diagram and pie chart. The mean difference between the continuous variables were analysed using paired t- test 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.

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Observations & Results:

Table 1: Age wise distribution of participants in the study

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

A total of 100 pregnant women with pre-eclampsia were included in study after obtaining the informed consent. The mean age of patients was found to be 25.47±5.58yrs. Majority of participants were in age group of 21-25yrs (38%) followed with 23% in age of 26-30yrs, 20% in 31-40yrs and 19% in 18-20yrs of age.

Table 2: Correlation of the result by urinary dipstick and urinary PCR with urinary 24hr protein estimation by Pearson's correlation

		24hr Urinary Protein
Spot Urinary Dipstick	R	0.896**
	Sig	.001
Spot Urinary PCR	R	0.976**
	Sig	.001
Spot Sulphosalicylic Acid Test	R	0.999**
	Sig	.001

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Table 3: Showing the AUC on ROC curve in predicting the significant proteinuria using different test method

Test Result Variable(s)	Area	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
Urinary Dipstick	.784	.001	.692	.877
Urinary PCR	.964	.001	.894	1.000
Sulphosalicylic Acid Test	.970	.001	.935	1.000

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

		24hr URINARY PROTEIN SIGNIFICANCE				
		<300mg		>300mg		Chi-square (p-value)
		Count	Column N %	Count	Column N %	
Spot Urinary Dipstick	Absent	1	4.5%	25	32.1%	6.74 (0.001)**
	Present	21	95.5%	53	67.9%	
Spot Urinary	<0.3	18	81.8%	1	1.3%	72.32

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PCR	>0.3	4	18.2%	77	98.7%	(0.001)**
Spot Sulphosalicylic Acid Test	<30mg/dl	21	95.5%	3	3.8%	84.615 (0.001)**
	>30mg/dl	1	4.5%	75	96.2%	

Table 5: Showing the diagnostic characteristics of urinary dipstick method

Spot Urinary Dipstick	Value	95% CI
Sensitivity	67.95%	56.42% to 78.07%
Specificity	4.55%	0.12% to 22.84%
Positive Predictive Value (*)	71.62%	67.88% to 75.09%
Negative Predictive Value (*)	3.85%	0.57% to 21.81%
Accuracy (*)	54.00%	43.74% to 64.02%

Table 6: Showing the diagnostic characteristics of urinary protein creatinine ratio method

Spot Urinary protein-creatinine ratio	Value	95% CI
Sensitivity	98.72%	93.06% to 99.97%
Specificity	81.82%	59.72% to 94.81%

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Positive Predictive Value (*)	95.06%	88.80% to 97.90%
Negative Predictive Value (*)	94.74%	71.77% to 99.22%
Accuracy (*)	95.00%	88.72% to 98.36%

Table 7: Showing the diagnostic characteristics of spot urinary Sulphosalicylic acid method

Sulphosalicylic acid test	**Value**	**95% CI**
Sensitivity	99.15%	89.17% to 99.20%
Specificity	95.65%	78.05% to 99.89%
Positive Predictive Value (*)	98.68%	91.68% to 99.80%
Negative Predictive Value (*)	88.00%	70.67% to 95.71%
Accuracy (*)	96.04%	90.17% to 98.91%

DISCUSSION:

Early identification of PE 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 examination during antenatal check-ups. Proteins in the urine signal the start of a hypertensive problem, either proteinuric gestational hypertension or superimposed preeclampsia on pre-existing renal illness. Amount of protein loss has diagnostic and prognostic ramifications, but what constitutes an ideal test is still debated.

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Nonpregnant women excrete minimal quantity of proteins in urine (150mg/day) but due to physiological changes that occur during pregnancy. protein excretion of 300mg/day is considered as abnormal.

This hospital based prospective clinical study was conducted among the pregnant women with more than 20 weeks of gestation diagnosed with pre-eclampsia and admitted to antenatal ward in department of obstetrics and gynaecology, Murshidabad Medical college, Berhampore, Murshidabad, West Bengal.

We aimed to compare different methods to quantify and estimate proteinuria in pre-eclampsia women and to find the best method for proteinuria estimation. proteinuria which is progressive indicates worsening of condition or disease and hence Proteinuria quantification is central to the investigation of hypertension in pregnancy which guides clinician in making decision and further planning of management.

In current obstetric practice, proteinuria was detected mainly by three methods such as sulphosalicylic acid test, dipstick test and urine spot protein-creatinine ratio. Till date 24h urinary protein excretion is considered as gold standard for estimation of protein. Moreover, this is costly, time consuming, cumbersome, errors in collection, difficulty in storage, difficulty in specimen storage, delay in diagnosis, poor patient compliance. This method is not useful in cases where urgent delivery is needed due to worsening of maternal and fetal condition.

Dipstick analysis which is simple, most popular, semi quantitative and readily available in hospitals, can be done by paramedical staff even by the patient which is usually advised as an admission test. However, inaccuracies in dipstick is due to diurnal variation, urinary tract infection etc.

Urine spot PCR in the random sample is slowly becoming popular as it gives fast and accurate results. It can be done on outpatient basis which will be very useful for the obstetrician for quick planning and management.

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 hr 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±5.58yrs.

Majority of participants were in age group of 21-25yrs (38%) followed with 23% in age of 26-30yrs, 20% in 31-40yrs and 19% in 18-20yrs of age. Among them majority were primigravida (64%), 345 were multipara. In similar to present study, Amin SV et al.[5], found the mean age of patients was 27.4±4.3yrs with minimum of 20yrs and maximum of 41yrs of age, and 51% women were primipara and 49% were Multipara by obstetric score.

Similar to present study Sharma et al[6] documented majority were in the age group of 21-30yrs of age (87.92%), followed with 7.9% in 31-40yr and 7.14% less than 20yrs of age.

In present study the mean SBP of 154.04±11.99mmHg and diastolic pressure of 100.52±7.39mmHg was observed. In concordance to present study, Amin et al.[5], documented the SBP of 152±18.2mmHg and DBP of 96.4±11.3mmHg in their study.

On correlation of the various estimations of spot urine protein with 24hr urinary total protein, we found a significant positive strength of association between them. The strong positive strength of association of SSA was higher compared to the spot urinary PCR and spot urinary

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dipstick result. The strength of association of SSA was r=0.999, p<0.05, urinary PCR was 0.976, p<0.05 and for spot urinary dipstick was 0.896, p<0.05. All the 3 methods of spot urine were strongly correlated with the SSA being superior followed with PCR and dipstick method.

In study by Archana K et al.[7] showed a significant strong correlation of spot UPCR with 24hr urinary proteinuria with r=0.88.

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 for the Sulphosalicylic acid was found to be significantly better (AUC=0.970, p<0.05) compared to the urinary PCR (AUC=0.964, p<0.05) and for urinary dipstick it was AUC=0.784, p<0.05.

The AUC of the SSA and urinary PCR was stronger than the urinary Dipstick method in correlation with 24hr urinary total protein estimation method.

In study by Berthet A et al.[10], the area under the curve for spot PCR was 0.92, with higher accuracy in diagnosing the proteinuria and thus pre-eclampsia.

In study by Sharma A et al.[6], documented the AUC for PCR was 0.793, p<0.05.

On assessment of diagnostic accuracy in term of sensitivity, specificity, PPV, NPV and accuracy of each method compared with the 24hr 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 SSA >>PCR>>Dipstick with accuracy of 96.04%, 95.0% and 54% respectively.

In study by Berthet A et al.[8], the result showed sensitivity of 79.3% and specificity of 91.5% for spot p/c ratio in accurate diagnosing the proteinuria and thus pre- eclampsia.

In study by Amin SV et al.[5], 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 cutoff value of 0.45.

Study by Sharma A et al.[6], The optimal spot P/C ratio cut off point was 0.2 for 300 mg/ 24 hr 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.

Study by Kayatas S et al.[9], study showed a significant correlation between 24hr urine protein excretion and urinary P/C ratio. The cut-off for P/C ratio was 300mg per 24hr was 0.28, with sensitivity of 60.4% and specificity of 77.9%. The study concluded that the spot P/C ratio is a poor predictor of 24hr proteinuria but can predict the proteinuria >2000mg better than 300-2000mg.

In study by Park JH et al.[10], concluded that that urine protein to creatinine ratio is a reliable indicator of significant proteinuria in preeclampsia and may be better at providing earlier diagnostic information than the 24-hour urine protein excretion with more accuracy than the urinary dipstick test.

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CONCLUSION:

This study concluded that spot urine sulphosalicylic acid and urine protein-creatinine ratio are reliable investigations compared to the dipstick method to assess the proteinuria in hypertensive pregnant women or for diagnosis of pre-eclampsia. So, spot urine Sulphosalicylic acid and urine protein-creatinine ratio can be used for detection of proteinuria in pregnant women with suspected 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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