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Original Research Article

Quantification of proteinuria by urine protein creatinine ratio in a single void urine in pre-eclamptic women and its correlation with 24 hours urinary protein

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ABSTRACT

Background: Proteinuria is a major indicator of hypertensive disorders of pregnancy. Though 24 hr urinary protein is considered to be the gold standard for evaluation of proteinuria in preeclampsia but its collection is time consuming, cumbersome and needs admission of the patient. The role of spot UPCR in random sample proposed as an alternative
Method: A observational cross-sectional study was conducted from 2020 to 2021 on 78 antenatal women of gestational age >20 weeks meeting the inclusion and exclusion criteria were enrolled into this study. Data was compared by using Pearson correlation coefficient (r). ROC curve was plotted for spot UPCR value for detecting significant proteinuria (>300 mg/24 hr).
Result: The quantification of proteinuria by spot UPCR strongly correlated with 24hr urinary protein. The p=0.001. There was a positive correlation of 24hr urine protein (mg/24 hr) with spot UPCR urine sample which was significant statistically (r=0.997, p<0.05) ROC curve analysis of Spot UPCR for proteinuria (>300 mg/24 hr) after the 20 weeks gestation. The spot UPCR showed significant large area under the curve (AUC) on the ROC curve. There is positive correlation between 24 hr urinary protein (>300 mg/24 hr) and spot UPCR in patients of pre-eclampsia
Conclusions: From our study we concluded that spot urinary protein creatinine ratio has a significant linear correlation with 24 hr urinary protein in pre-eclampsia.

Keywords: Spot UPCR, Proteinurea, Pre-eclampsia

INTRODUCTION

Hypertensive disorders of pregnancy are the leading causes of maternal and perinatal mortality and morbidity globally. It has been estimated that preeclampsia complicates 2-8% of pregnancies worldwide.[1] However, in India, the incidence of pre-eclampsia is 5-10% and it is more common in primigravida (approximately 16%) as compared to multigravida (7%).[2,3] Overall prevalence of hypertensive disorder in pregnancy is 8.6%.[4] Increased prevalence of predisposing disorders such as chronic hypertension, diabetes and obesity are responsible for increased incidence of preeclampsia in developed countries.[5] According to a study by Rastogi et al the prevalence of hypertensive disorders of pregnancy in India is 7.8% and out of which 5.4% is due to pre-eclampsia.[6]

Pre-eclampsia is multisystem endothelial disease that leads to glomerulo-endotheliosis, and in severe cases it may lead to renal impairment and failure.[7] Tubular permeability is increased in preeclampsia, which leads to nonselective proteinuria to most large molecular weight proteins (albumin, globulin, transferrin, and hemoglobin). So, detection of proteinuria is crucial to management of pre-eclampsia as it signifies higher rate of adverse feto-maternal outcome.[8,9] Presence of significant proteinuria (in addition to hypertension) predisposes pregnant woman to coagulopathy, liver disease and stroke. Serious perinatal

morbidity occurs in form of preterm delivery (often iatrogenic) and fetal growth restriction.[10] Proteinuria, one of "cornerstones" of antenatal care, is major indicator of hypertensive disorders of pregnancy. Though, 24 hrs urinary proteins are considered to be gold standard for evaluation of proteinuria in preeclampsia but its collection is time consuming, cumbersome and needs admission of patient.[11] A need for an accurate, quick and acceptable test arises so that an early diagnosis is made.

Present study was conducted to compare the results of 24-hour urinary protein and spot urine protein creatinine ratio in clinically diagnosed cases of pre-eclampsia and to compare the diagnostic accuracy of these two tests for prediction of significant proteinuria.

METHODS

This was a tertiary hospital based observational cross-sectional study, which was conducted on antenatal women with pre-eclampsia who attended antenatal OPD/admitted in the department of obstetrics and gynaecology at Hindu Rao hospital, Delhi in close association with department of biochemistry from September 2020 to August 2021. This study was carried on randomly selected antenatal cases with pre-eclampsia of more than 20 weeks gestation (as defined by ACOG 2017) and who were willing to participate in the study. Patients with history of pre-existing renal, vascular or heart disease/ with recurrent urinary tract or vaginal tract infection or who used vulval or vaginal antiseptics or skin cleanser were excluded from study. Patients who required delivery before completion of 24 hr urine sample/who had pre-labour rupture of membranes were also excluded from study. Samples containing red blood cells or pus cells were rejected.

Sample size was calculated by taking into consideration the prevalence of antenatal women with pre-eclampsia, with allowable error of 5%. It was calculated by using the formula $n=(Z^2\times P\times Q)/ r^2$. Where Z=1.96, P=prevalence (5.4), Q=1-prevalence, r=5, allowable error. Thus, study was comprised of at least 80 antenatal women with preeclampsia presenting to department of obstetrics and antenatal OPD, Hindu Rao hospital. After explaining procedure to patient and getting informed consent a proforma was filled with all details of patient and she assured for confidentiality. Detailed history of patient including age, demographic profile, history of present illness, menstrual history, obstetrics history, past history and family history was taken. After that general examination, systemic and obstetric examination done. The patients were instructed to collect the 24 hours urine starting from the second urine sample in the morning till the first urine sample next day morning. Each container was marked with patient name, MRD number and collection time. Patient was instructed to avoid cleaning with antiseptics or skin cleansers. Another mid-stream urine sample for spot urine protein/creatinine ratio estimation was taken at the same time.

Statistical analysis

The data thus collected was analysed using appropriate statistical methods with statistical software SPSS version 27.0 where $p<0.05$ is statistical significant. Study received ethical clearance from institutional ethics committee.

RESULTS

Table 1, shows the demographic and biochemical data of the patients with pre-eclampsia enrolled in our study**.** In our study there were 20 patients who had signs and symptoms (S/S) of impending eclampsia (headache, blurring vision, epigastric discomfort etc) while 50 patients had no S/S of impending eclampsia. Table 2 shows the correlation of clinical and biochemical data with sign and symptoms (S/S) of Impending Eclampsia. The comparison of mean systolic and diastolic blood pressure, mean of 24 hr urinary protein and spot UPCR, mean blood urea and serum creatinine, mean liver function test in patients with and without S/S of impending eclampsia was statistically significant. Table 3 and Figure 1, show correlation of the 24-hour urine protein (mg) and spot urinary protein creatinine ratio spot (UPCR) which was significant statistically ($r=0.997$, $p<0.05$).

Table 4 (A) shows the sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) of 24hour urinary protein (mg/24 hr) test and spot UPCR test in patients of pre-eclampsia in relation to development of S/S of impending eclampsia. Table 4 (B) shows the receiver operating characteristic (ROC) analysis of 24 hr urinary protein and spot UPCR in relation to S/S of impending-eclampsia. Figure 2 and 3 show a significant large area under the curve for 24 hr urinary protein and spot UPCR (AUC=0.836 and 0.849 respectively) on the ROC curve which is expressed as a solid line in relation to S/S of impending-eclampsia.

Table 1: Demographic and biochemical data in patients of pre-eclampsia.

Variables	Mean	±SD	Minimum	Maximum	Median
Age (In years)	26.59	3.67	19.00	35	27
Gestational age (weeks)	35.76	2.96	26.20	40.30	36.50
Systolic BP (mmHg)	155.71	7.51	142.00	180.00	155.00
Diastolic BP (mmHg)	102.7143	4.6692	94.00	112.00	102.00
24 hr urinary protein (mg/24 hr)	686.9571	738.9829	280.0000	4269.00	405.50
Spot UPCR	0.6744	0.7328	0.2800	4.3100	0.3900
Blood urea(mg%)	42.0286	13.9117	23.0000	87.0000	37.00000

Continued.

Variables	Mean	±SD	Minimum	Maximum	Median
S. creatinine (mg%)	0.8837	0.1424	0.6500	1.3000	0.8700
SGOT	129.7286	104.5272	25.0000	413.0000	97.0000
SGPT	135.2143	107.3276	25.0000	415.0000	90.5000

Table 2: Comparison of clinical and biochemical data vs S/S of impending eclampsia.

Variables	S/S of impending eclampsia				P value
	Absent, (n=50)		Present, (n=20)		
	Mean	± SD	Mean	± SD	
Systolic BP (mmHg)	153.28	6.79	161.80	5.58	<0.0001
Diastolic BP (mmHg)	101.48	4.20	105.80	4.44	<0.0001
24 hr urinary protein (mg/24 hr)	444.76	275.07	1292.45	1117.03	<0.001
Spot UPCR	0.44	0.26	1.27	1.12	<0.001
Blood urea (mg%)	37.66	11.75	52.95	13.08	<0.001
S. creatinine (mg%)	0.84	0.12	1.00	0.13	<0.001
SGOT(IU)	84.94	66.83	241.70	98.40	<0.001
SGPT(IU)	86.48	56.77	257.05	107.92	<0.001

Table 3: Correlation of the 24 hr urine protein and spot UPCR urine sample.

Variables	Karl-Pearson's correlation coefficient	P value
24-hr urine protein and spot UPCR	0.997	<0.001

Significant (<0.05)

Table 4 (A): Sensitivity, specificity, negative and positive predictive value for the 24 hr urinary protein (mg/24 hr) and spot UPCR test against the S/S of impending eclampsia.

Test	Cut point of spot PCR	Sensitivity	Specificity	PPV	NPV
24 hr urinary protein (mg/24 hr)	405 (median)	56.0%	65.0%	80.0%	37.1%
Spot UPCR	0.39	50.0%	70.0%	80.6%	35.9%

Table 4 (B): ROC analysis of S/S of impending eclampsia.

Variables	Area	Std. error	Significant	95% CI	
				Lower bound	Upper bound
24 hr urinary protein (mg/24 hr)	0.836	0.057	0.000	0.724	0.947
Spot UPCR	0.849	0.051	<0.001	0.750	0.948

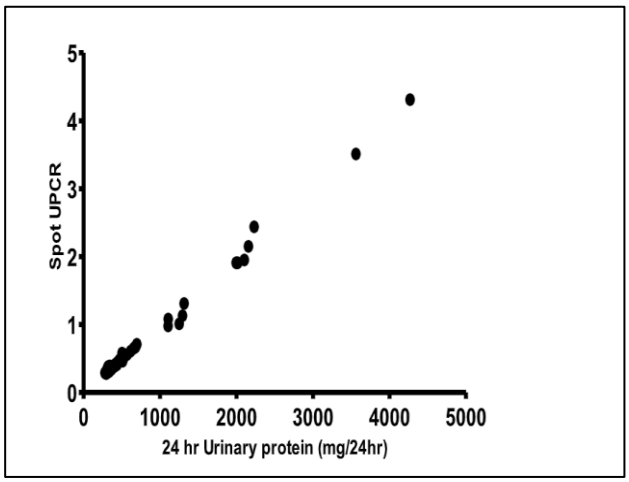

Figure 1: Correlation between 24-hour urine protein and spot UPCR urine sample.

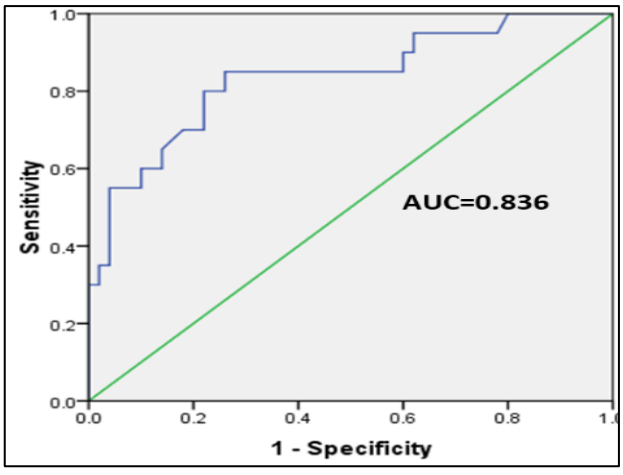

Figure 2: ROC curve analysis of 24-hour urinary protein (mg/24 hr) for impending eclampsia

screening. Each receiver characteristic curve is expressed as a solid line.

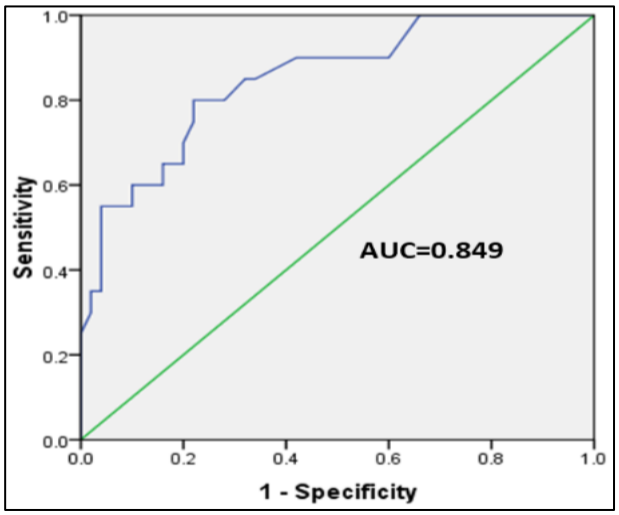

Figure 3: ROC curve analysis of spot UPCR for impending eclampsia screening. Each receiver characteristic curve is expressed as a solid line.

DISCUSSION

Pre-eclampsia is a leading cause of maternal and fetal morbidity and mortality, so testing of proteinuria is one of the diagnostic criteria of pre-eclampsia. The gold standard testing of proteinuria detection is 24 hr urinary protein, which is time consuming and cumbersome. It is not always performed correctly and can cause delayed diagnosis and treatment, so spot urine protein creatinine ratio developed as an alternative test due to high accuracy, reproducibility and convenience. So, this cross-sectional study was conducted on 70 admitted antenatal cases of pre-eclampsia in the department of obstetrics and gynecology at Hindu Rao hospital to study the relationship between spot urinary protein creatinine ratio and the 24 hour urinary protein for proteinuria in pre-eclampsia.

In our study, the mean age of the patients was 26.59±3.67 years with range from 19 to 35 years, which is comparable to the study done by Demirci et al.[12] The mean maternal age in their study was 28.2±5.5 years. The mean gestational age was 35.76±2.96 weeks with maximum and minimum gestational age range of 26.20 to 40.30 weeks. It is comparable with the study done by Obeid et al where it was 35 weeks with range 20.6 to 41.1 weeks.[13] The mean gestational age was 37.27±1.83 weeks in the study Jan et al.[14]

In our study, the mean systolic BP was 155.7143±7.5087 mmHg in patients of pre-eclampsia, with range from 142 to 180 mmHg. The mean diastolic BP of patients of pre-eclampsia was102.7143±4.6692 mmHg with minimum and maximum Diastolic BP as 94.0 mmHg and 112.0 mmHg respectively. It is comparable with the study done by Rizk et al.[15] The mean systolic BP in their study was 153.3±12.9 mmHg with range from 130 to 170 mmHg and mean diastolic BP was 97.2±8.2 mmHg with range from 90 to 110 mmHg.

In our study, the mean 24 hr urinary protein of patients of pre-eclampsia was 686.9571 mg/24 hr with range from 280 mg/24 hr to 4269 mg/24 hr. The median 24 hr urinary protein in these patients was 405.50 mg/24 hr. In contrast in the study by Nigam et al the mean 24 hr urinary protein was 1704.39±1338.94 mg/24 hr while Demirci et al showed mean urinary protein as 2801.8±3009 mg/24 hrs and median urinary protein level as 2.8 gm (range 0.3-18.8) in 24-hour urinary protein excretion.[12] The mean spot UPCR of patients of pre-eclampsia was 0.6744 with minimum and maximum at 0.2800 to 4.31 respectively. The median spot UPCR in these patients was 0.3900. In contrast in the study by Nigam et al the mean spot UPCR was 1.96±1.54. While Demirci et al showed mean spot UPCR as 3±3.8 and median spot UPCR as 2.96 (range 0.15-29.6).[12]

In our study the mean blood urea of patients of pre-eclampsia was 42.0286±13.19 mg% with range from 23 to 87 mg%. The median blood urea in these patients was 37. It is comparable with study by Jan et al where the mean blood urea was 30±5.6 mg%. The mean serum creatinine was 0.8837±0.14 mg% with range from 0.6500 to 1.300 mg%. The median serum creatinine in these patients was 0.87 mg%. It is comparable with study by Jan et al and Demirci et al who showed mean serum creatinine values as 0.9±0.2 and 0.64±0.4 mg% respectively.[12]

In our study mean 24 hour urinary protein (mean ± SD) of patients without S/S of impending eclampsia was 444.76±275.07 mg/24 hr and the mean 24 hour urinary protein (mean±SD) with S/S of impending eclampsia was 1292.45±1117.03 mg/24 hr and the difference of mean 24 hr urinary protein in the two groups was statistically significant ($p<0.001$).Also mean spot UPCR (mean ± SD) of patients without S/S of impending eclampsia was 0.44±0.26 mg% and in 20 patients with S/S of impending eclampsia the mean spot UPCR (mean±SD) was 1.27±1.12 mg%. Distribution of mean spot UPCR in patients with and without S/S of impending eclampsia was statistically significant ($p<0.001$).

In our study shows that mean SGOT (mean ± SD) of patients with S/S of impending eclampsia was 241.70±98.40 IU and in patients without S/S of impending it was 84.94±66.83 IU. Distribution of mean SGOT with S/S Of impending eclampsia was statistically significant ($p<0.001$) and mean SGPT (mean ± SD) of patients with S/S of impending 257.05±107.92 IU and without S/S of impending eclampsia was 86.48±56.77 IU. Distribution of mean SGPT with S/S of impending eclampsia was statistically significant ($p<0.001$).

There was a positive correlation of 24-hour urine protein (mg/24 hr) with spot UPCR urine sample which was significant statistically (coefficient of correlation: r=0.997,

p<0.001). Study by Nigam et al also showed a strong correlation between 24 hour urinary protein and spot UPCR for values between 0.3 to 3.0, and the results was statistically significant (coefficient of correlation: r=0.851, p<0.001).[16] Comparable studies done by Shahbazian et al had strong correlation between the spot urine protein creatinine ratio and 24-hour urine protein excretion (r=0.84; p<0.001).[17] Another study by Jan et al significantly correlation (r=0.824 p<0.0001) was found between spot urine protein/creatinine ratio and the 24-hours protein excretion.[14]

In our study the sensitivity, specificity, NPV and PPV were calculated for analysis of proteinuria (>300 mg/24 hr) after the 20 weeks by spot PCR test in patients of pre-eclampsia as shown in Table 3. The cut-off value for spot UPCR was 0.30 to make a diagnosis of severity of proteinuria (>300 mg/24 hr). With these cut-off values, spot UPCR had sensitivity of 80% and specificity of 100% and PPV of 100% and NPV of 98.5% in the diagnosis of severity of disease. These tests were demonstrating the accuracy of risk factors. It is comparable with the study done by Obeid et al, Demirci et al, Jan et al and Rizk et al at cut-off of 0.03 the sensitivity, specificity, PPV and NPV are shown in the following table.[13-15]

CONCLUSION

From our study we concluded that spot urinary 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 spot urine protein creatinine ratio can be used as an excellent alternative for the time consuming 24 hour urinary protein estimation in patients with pre-eclampsia.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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