

Correlation of 24-hour urinary protein excretion and spot urine protein-creatinine ratio in women with preeclampsia: A cross sectional study

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Abstract

Objective: To examine the correlation between spot urine PCR and 24-hour urine protein excretion in patients being evaluated for preeclampsia. **Material and Methods:** A cross sectional study was conducted on 100 patients at the Department of Obstetrics and Gynecology at Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar, Telangana State for a period from December 2019 to August 2020, with inclusion of singleton viable pregnancy, Gestational age between 24 and 38 weeks, Confirmed by last menstrual period and early ultrasound. **Result:** Among 100 patient's patients having mean age of 25 ± 3.266 years, among the patients 19% percent of the patients had past history of preeclampsia. Mean gestational age for the patients was 32.39 ± 3.42 weeks. Study showed 62 % of moderate urinary protein levels. There was significant correlation between spot PCR and 24 hour urine protein collection (spearman's $\rho=0.7$, $P<0.0001$). **Conclusion:** Urine protein: creatine ratio is one of the important investigation in hypertensive disorder of the pregnancy. Spot Urine protein: creatine ratio can reliably be taken as a simple, accurate, and convenient replacement for tedious, time consuming 24 hour urine protein estimation, especially in countries like India where hospitals are flooded with a large number of in-patients. Therefore Urine protein: creatine ratio estimation should be introduced and adopted in practice in testing for proteinuria.

Keywords: Preeclampsia, protein: creatine ratio, Dipstick, Proteinuria

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INTRODUCTION

Preeclampsia (PE) is disorder of pregnancy which is characterized by the beginning of high blood pressure and more amount of protein the urine. The condition of preeclampsia begins after 20 weeks of pregnancy, it affects 2% to 8% of pregnancies and is a major contributor to fetal, neonatal, and maternal morbidity and mortality.

Preeclampsia symptoms might be revealed from 20 weeks of gestation up to six weeks postpartum and is considered early onset before 34 weeks of gestation^{1,2} Proteinuria occurs in preeclampsia as a consequence of reduction in the integrity of glomerular barrier or reduced tubular reabsorption. Proteinuria is one of the signs of preeclampsia which is defined as >300mg of protein in a 24- hour urine collection. Estimation of proteinuria is essential for making diagnosis, to assess the severity of disease and also for predicting fetal maternal outcome in preeclamptic pregnancies. For estimating the amount of protein in urine collection of 24 hour urinary sample is taken as gold standard, but it is time consuming, cumbersome and inconvenient. There is a need for a quick, reliable, acceptable and cost effective alternative test. Several methods for proteinuria evaluation are available in daily practice: (1) dipstick, (2) 24 h urine protein test, and (3) urine protein-to-creatinine ratio (UPCR). The spot protein creatinine ratio (PCR) has been proposed as an

alternative test for the diagnosis of preeclampsia [3,4]. In this method urinary protein concentration is divided by GFR independent urinary creatinine concentration. Therefore it is a useful reference and considered to be a reliable indicator of proteinuria. Result for this test is available in very short time and help practitioners for quick decision and management planning. So in the present study we are going to examine the correlation between spot urine PCR and 24-hour urine protein excretion in patients being evaluated for preeclampsia

MATERIAL AND METHODS

A cross sectional study was conducted at the Department of Obstetrics and Gynecology at Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar, Telangana State for a period from December 2019 to August 2020 and was approved by Institutional Ethical Committee of our institute. Total of 100 patients with preeclampsia of the pregnancy were recruited after 20 weeks of gestation and these patients had detailed medical and obstetrical history, general physical and systemic examinations, and other investigations required for the management.

Inclusion criteria:

1. Singleton viable pregnancy
2. Gestational age between 24 and 38 weeks
3. Confirmed by last menstrual period and early ultrasound.

Exclusion criteria:

1. Multiple pregnancies
2. Diabetes mellitus
3. Chronic hypertension
4. preexisting renal disease
5. Abnormal fetus
6. Urinary tract infection
7. overt diabetes mellitus

Estimation of 24 Hours Urinary Protein:

Patients were instructed to collect urinary sample for 24 hours in our lab, quantitative estimation of proteinuria was done by turbimetric method using sulphosalicylic acid. The advantage is this can be easily performed. It will detect other proteins such as globulin and Bence Jones protein in addition to albumin. Total 24-hour urinary volume is measured and the adequacy of sample was cross checked with creatinine in the sample to the predicted creatinine concentration. 0.5 ml of urinary sample is taken to this 2 ml of 3% sulphosalicylic acid is added. It forms a white turbid sample depends on the amount of protein. It is measured using Auto Colorimeter Model No:1000 at Optical Density 640 nm. Eg) If OD is 0.05 the amount of protein is 8 mg/ dl likewise a standard method is followed.

Total 24 hour Urinary Protein

$$\frac{\text{Urinary Protein Concentration mg/dl} \times 24 \text{ hr urinary volume in ml}}{100}$$

Urinary spot protein creatinine ratio

Urinary protein concentration is measured by Sulphosalicylic acid method. Estimation of urinary creatinine is based on Jaffes principle. On addition of picric acid to the urinary creatinine at alkaline pH it forms an orange colour creatinine alkaline picrate. The magnitude of change in colour is measured using colourimeter at 492nm. The creatinine concentration is calculated by calibrating against solution of known creatinine. Urinary PCR is calculated by dividing urinary protein concentration by urinary creatinine concentration. All the data collected from procedures has entered in the Microsoft excel 2010 for further analysis and presentation of data. Quantitative data were presented by using Mean and Standard Deviation. Linear regression model were used to know the correlation between the two tests. ROC curve to know comparison between the tests. Statistical packages for social science (SPSS) version 25 were used for statistical analysis and p-value<0.05 were considered as statistical significant.

RESULT

In the given study of 100 patients mean age of all patients was 25 ± 3.26 Years, mean gestational age (Weeks) 32.39 ± 3.42, mean Systolic Blood Pressure was 157.5 ± 16.9mmhg and diastolic was 99 ± 8.587 mmhg, among the patients contribution of primigravida and multigravida were 46% and 54% respectively. There were 19% of the patients who had history of preeclampsia. Shown in table number 1.

Table 1: General characteristic of study Population

| Parameter | Mean ± SD/No. | Range /Percentage |
|------------------------------|---------------|-------------------|
| Age (Years) | 25 ± 3.266 | 19 - 34 |
| GA (Weeks) | 32.39 ± 3.42 | 24 - 38 |
| SBP (mmHg) | 157.5 ± 16.9 | 110 - 210 |
| DBP(mmHg) | 99 ± 8.587 | 90 - 120 |
| Gravida | | |
| Primi | 46 | 46 |
| Multi | 54 | 54 |
| Past H/O Preeclampsia | | |
| Yes | 19 | 19 |
| No | 81 | 81 |

24-hour urine protein estimation was done, in which 20 patients (20%) had insignificant proteinuria of less than 300mg/day which is a defined cutoff pregnant women. 62% (62/100) had moderate proteinuria raging between

300mg and 2000mg and of them 18 (18%) had severe proteinuria means more than 2000mg/day. Shown in Table. 2

Table 2: 24 Hours urinary protein urea level of study Population

| 24 Hours Urinary Protein | Frequency | Percent |
|--------------------------|------------|------------|
| Mild (<300) | 20 | 20 |
| Moderate (300 - 2000) | 62 | 62 |
| Severe (> 2000) | 18 | 18 |
| Total | 100 | 100 |

The mean protein excretion per day were 1182.55 mg with standard deviation of 1492.033mg, respectively, ranging between 122 – 6320mg/day.

Table 3: Descriptive statistics of 24 hours urinary protein and spot protein/creatinine ratio of study Population

| Measure | P/C Ratio | 24 Hours Urinary collection for Protein |
|----------------|-------------|---|
| No | 100 | 100 |
| Mean ± SD | 1.20 ± 1.49 | 1182.55 ± 1492.033 |
| Standard Error | 0.149 | 149.203 |
| Mode | 0.45 | 980 |
| Range | 0.11 - 63 | 122 - 6320 |
| Percentile | | |
| 5th | 0.12 | 125 |
| 25th | 0.41 | 405 |
| 50th | 0.55 | 549.5 |
| (Median) | | |
| 75th | 0.98 | 980 |
| 90th | 4.35 | 3980 |
| 95th | 4.69 | 4715 |

The area under the receiver operating characteristic (ROC) curve for PCR was 0.88 (95% CI 0.81-0.96) this was statistically significant P<0.0001 (Figure 2). There was significant correlation between spot PCR and 24 hour urine protein collection (spearman’s rho=0.7, P<0.0001) (Figure 1).

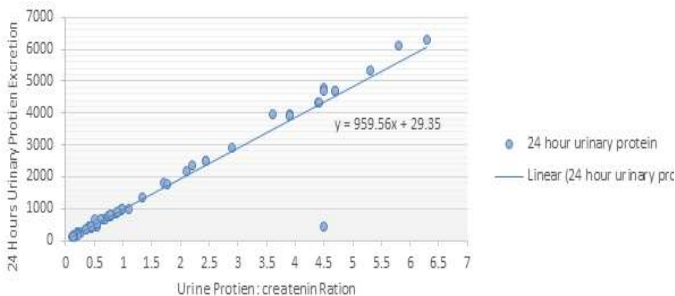


Figure 1: Correlation between 24 hours urinary protein and spot protein/creatinine ratio of study Population

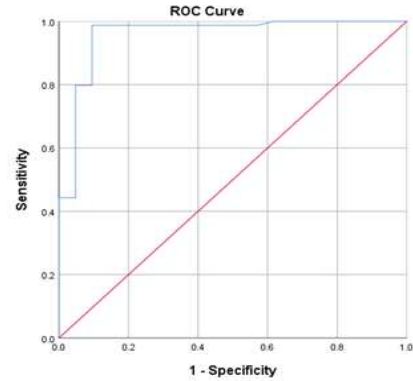


Figure 2: Receiver operating curve of 24 Hours urinary protein

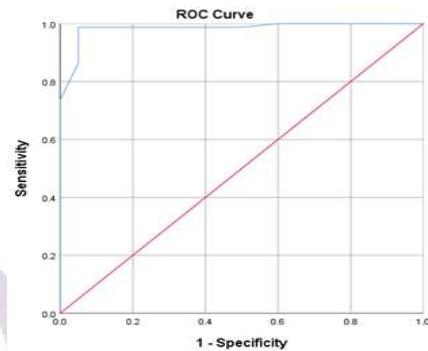


Figure 3: Receiver operating curve of Spot urinary protein creatinine ratio

The ROC curve plot sensitivity (true positive rate) against 1 – specificity (true negative rate). The area under curve was calculated, it was 0.984 for P/C ratio with [95% confidence interval (95% CI), 0.960–1.00] shown in figure 3. For random P/C ratio at various cut-offs for prediction of significant and severe proteinuria, the cutoff point in current study was (0.1750), with sensitivity of (98.8%) and specify of (50%). Analysis of the ROC curve indicated that a random urine P/C ratio of 0.1750 was the best cutoff point to detect severe proteinuria in women with PE.

DISCUSSION

Since time immortal, urine examination remains one of the important examinations during antenatal checkups. The finding of significant proteinuria is an essential component in the diagnosis of preeclampsia with its risk of maternal and perinatal morbidity and mortality. Early diagnosis and treatment of preeclampsia is essential for prevention of eclampsia. Preeclampsia is an endothelial disease that leads to glomeruloendotheliosis and in severe cases it may lead to renal impairment and failure. Increase permeability of the glomerular basement membrane leading to proteinuria⁵. On the other hand accurate diagnosis is important to prevent unnecessary interventions in hypertensive pregnant women, whether further testing or

treatment. Three methods of urine protein estimation have been used amply in the current obstetric practice. Most popular one is urine dipstick analysis which is readily available in most of the hospitals and is also semi-quantitative, the second one is so called “gold standard” 24 hours urinary proteins but is limited by its availability and time constraints, and the third one is slowly becoming popular, that is, the estimation of ratio of either protein or albumin to the creatinine concentration (urinary protein : creatine ratio (UPCR) and urine albumin : creatinine ratio (UACR)) in the random urine sample. This method gives faster and reasonably accurate assessment of significant proteinuria.⁶ Present study was conducted to evaluate the correlation between spot urine PCR and 24-hour urine protein excretion in patients being evaluated for preeclampsia. The following studies agree with our study in demonstrating correlation between the 24 hours urine protein and the protein/creatinine ratio. Our study of 100 hypertensive pregnant women, that the random urine p/c ratio was strongly correlated to 24h urine protein excretion with ($r=0.70$, $P<0.001$). A cut off value of 0.172mg/mg for P/C ratio best predicted significant proteinuria with sensitivity, specificity, of 98.8%, 50%, respectively. A Study conducted by Miami A. Ali *et al.* (2015)⁷ showed that there was significant correlation between P/C ratio in a single void urine with 24 hour urine collection for protein as the P value was (0.0001), The ROC curve analysis showed an area under the curve of (0.879), indicating that the urine P/C ratio can detect significant proteinuria, and to detect severe proteinuria at a cutoff point of 4.2 with a sensitivity of (81.8%) and specificity of (85.2%). Another study conducted by In study conducted in 2013 by Takahiro Yamada *et al.*⁸ found in their study that a single void p/c ratio practically better than 24hour and more acceptable by the patients, we also found that in our study. R K Morris *et al.* 2012⁹ found in their study that the threshold values for P/C ratio ranged between 0.13 and 0.5, with estimates of sensitivity ranging from 0.65 to 0.89 and estimates of specificity from 0.63 to 0.87; the area under the summary receiver operating characteristics curve was 0.69. Eslamian L *et al.* 2011¹⁰ reported in their study which include 100 hypertensive pregnant women, that the random urine p/c ratio was strongly correlated to 24h urine protein excretion with ($r=0.777$, $P<0.001$). A cut off value of 0.22mg/mg for P/C ratio best predicted significant proteinuria with sensitivity, specificity, of 87%, 92.6%, respectively. N. Aggrawal MD *et al.* 2008¹¹ found in their study which included 120 patients with PE constituted their study group, the area under the ROC curve was 0.79 (95% CI 0.67–0.91), with a cut off P/C ratio greater than 1.14 as a predictor of significant proteinuria, sensitivity and specificity were 72% and 75%, respectively. Ali and Navin Jaipaul found that the random urine P:C ratio is a

reliable and practical way of estimating and following proteinuria, but its precision and accuracy may be affected by the level of patient physical activity.¹² Young *et al.*... found no single value to distinguish significant proteinuria after ROC analysis but found a value of less 0.15 g/g efficiently ruled out pregnancy induced hypertension¹³. A study by Lamontagne showed a variation in PCR result during the day, in their study PCR was less sensitive in first morning samples¹⁴. The limitations of the present study were the low sample size, and the difficulties in collection of 24 hours urine sample in the female patients. Further study is required with large sample size to emphasize the hypothesis. False negative results is most important thing in clinical practice for this test, in our study we maximized the sensitivity at the expense of specificity, to reduce the possibility of missing the diagnosis of preeclampsia, as a false positive PCR would not lead necessarily to interventions in the absence of other findings.

CONCLUSION

Urine protein: creatine ratio is one of the important investigation in hypertensive disorder of the pregnancy. It is simple, accurate, and convenient measurement. There is a significant correlation between the spot urine P/C ratio and 24-hr urine protein excretion in women with preeclampsia. Random urine P/C ratios can be used as a reasonable alternative to 24-hr urine protein excretion for exclusion of Preeclampsia, especially in emergent situation. Spot Urine protein: creatine ratio can reliably be taken as a simple, accurate, and convenient replacement for tedious, time consuming 24 hour urine protein estimation, especially in countries like India where hospitals are flooded with a large number of in-patients. Therefore Urine protein: creatine ratio estimation should be introduced and adopted in practice in testing for proteinuria.

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Conflict of interest: None to declare.

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