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Original Research Article

## A study of spot urine protein: creatinine ratio as an alternative to 24 hours proteinuria for the diagnosis of pre-eclampsia

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### ABSTRACT

**Background:** Preeclampsia is defined as systolic blood pressure level of 140 mmHg or higher or a diastolic blood pressure level of 90 mmHg or higher that occurs after 20 weeks of gestation with proteinuria. Objective of this study was to study the role of spot urine protein: creatinine ratio as an alternative to 24 hours proteinuria for the diagnosis of pre-eclampsia

**Methods:** This is a prospective observational study conducted in the department of obstetrics and gynaecology, BRD Medical College Gorakhpur, since October 2016 to September 2017 included 120 pregnant women with hypertension of gestational age more than 20 weeks. Random urine sample of all the patient was taken before 12 noon after first voiding. For 24 hours urine sample patient was asked to collect all her urine she voids during 24 hours. The creatinine was estimated by the alkaline picrate method (Jaffe's Reaction) modified by the Bonsnes and Tausky, 1945. Creatinine in a protein free solution reacts with the alkaline picrate and produces red colour complex which is measured colorimetrically. Urinary protein was estimated in all the subjects by the Turbidimetric method. Urinary protein was precipitated by 3% sulphosalicylic acid and turbidity so produced was measured colorimetrically.

**Results:** Protein: creatinine ratio in a random urine sample is better than random urine protein detection by dipstick method in cases of emergency when there is no time for detection of 24 hours urine protein.

**Conclusions:** If cut-off level for urine protein: creatinine ratio in random urine sample is taken as 0.25 or more then sensitivity and specificity become same as 24 hours urine protein.

**Keywords:** Eclampsia, Fetal growth restriction, Gestational age, Pedal edema, Pre-eclampsia, Protein: creatinine ratio, 24 hours urine protein

### INTRODUCTION

Preeclampsia is defined as systolic blood pressure level of 140 mmHg or higher or a diastolic blood pressure level of 90 mmHg or higher that occurs after 20 weeks of gestation with proteinuria. Preeclampsia is an important cause of maternal morbidity and mortality as well as a significant contributor to increased perinatal morbidity and mortality rates in India, 12% of all maternal deaths

worldwide are due to hypertensive disorders of pregnancy. Proteinuria is defined as presence of 300 mg or more protein in a 24-hour urine specimen.<sup>1</sup>

There are many different causes for the condition. It appears likely that there are substances from the placenta that can cause endothelial dysfunction in the maternal blood vessels of susceptible women. While blood pressure elevation is the most visible sign of the disease.

It involves generalised damage to the maternal endothelium, kidneys and liver with the release of vasoconstrictive factors being a consequence of the original damage.

The pre-eclampsia syndrome is thought in many cases to be caused by a shallowly implanted placenta which becomes hypoxic, leading to an immune reaction characterized by secretion of unregulated inflammatory mediators from the placenta, and acting on the vascular endothelium

### **Diagnosis**

*Pre-eclampsia is well diagnosed when a pregnant woman develops*

Blood pressure >140 systolic and/or >90 diastolic (two separate readings taken at least four hours apart) and 0.3 grams or more of protein in a 24-hour urine sample (proteinuria) or  $\geq 1$  persistent dipstick.

*Criteria for diagnosis of severe pre-eclampsia*

- Systolic blood pressure of 160 mmHg or higher or diastolic 110 mmHg or higher on two occasions at least 4 hours apart while the patient is in bed.
- Proteinuria of 5 gram or higher in 24 hours urine specimen or 3+ or greater on two random urine samples collected at least 4 hours apart
- Oliguria of less than 500 ml in 24 hours
- Cerebral or visual disturbances
- Pulmonary edema or cyanosis
- Epigastric or right upper quadrant pain
- Impaired liver function
- Thrombocytopenia
- Fetal growth restriction.<sup>2</sup>

Swelling or edema (especially in the hands and face) was originally considered an important sign for a diagnosis of pre-eclampsia, but in current medical practice only hypertension and proteinuria are necessary for a diagnosis. Pitting edema (unusual swelling, particularly of the hands, feet, or face, notable by leaving an indentation when pressed on) can be significant and should be reported to a health care provider.<sup>3</sup>

Urine collection over 24 hours is considered the traditional Parameter for quantification of proteinuria in pregnancy. As 24 hours urine collection is difficult to patient so we have alternative method for quantitative evaluation of proteinuria is the measurement of protein: creatinine ratio in a spot urine sample, which provides a more convenient and rapid method to assess protein excretion.<sup>4</sup>

The dipstick is inexpensive, easy to use, and provides a rapid result but has been shown to have low sensitivity

and specificity for urinary protein excretion over 24 hours.

Recently, the urine protein-creatinine ratio has been considered important for predicting proteinuria in pregnant patients. It compares the spot urine protein excretion to the spot urine creatinine excretion, thereby normalizing protein excretion to the glomerular filtration rate. Thus, the urine protein-creatinine ratio is not subject to variation due to hydration status. In pregnant women, the urine protein-creatinine ratio and the 24 hours urine are highly correlated. We carried out a systematic review to assess the diagnostic value of protein: creatinine ratio in a single voided urine sample compared with 24 hours urinary collection for the detection of significant proteinuria in hypertensive pregnant women attending the antenatal clinic or admitted in the antenatal ward.<sup>5</sup>

Objective of this study was to study the role of spot urine protein: creatinine as an alternative to 24 hours proteinuria for the diagnosis of pre-eclampsia.

### **METHODS**

This study was conducted in the department of obstetrics and gynaecology, BRD Medical College Gorakhpur, from October 2016 to September 2017 includes cases pregnancy with hypertension.

#### **Inclusion criteria**

- Study population consisted of admitted antenatal cases of gestational age >20 weeks with raised blood pressure.

#### **Exclusion criteria**

- Women with known kidney disease, Bacteriuria, Bed rest longer than 24 hours, Gestational diabetes mellitus, women who delivered their babies during the urine collection, known patients on immunotherapy, immune compromised individuals, multiple pregnancy are excluded.

The 24 hours proteinuria and spot urine protein creatinine ratio will be recorded.

#### **Statistical analysis**

Student's t-test will be applied using SPSS software.

### **RESULTS**

In the mentioned (Table 1), out of total 120 patients 96 were detected as pre-eclampsia and had significant proteinuria. Among them 84 had proteinuria in the range of 0.3-1.5. Only 4 had proteinuria 0.3 gm/24 hours and 8 had proteinuria in the range of 1.6-2 gm/24 hours.

**Table 1: Distribution of patients according to 24 hours urine protein.**

24 hours urine protein (gm/24 hours)	Number of cases	Percentage (%)
< 0.3	24	20%
0.3	4	3.33%
0.3-1.5	84	70%
1.6-2	8	6.66%
<b>Total = 120</b>	<b>120</b>	<b>100%</b>

**Table 2: Distribution of patients according to protein: creatinine ratio in spot urine.**

Protein : creatinine ratio in spot urine sample	Number of cases	Percentage (%)
0.12-0.2	24	20%
0.25	4	3.33%
0.25-0.43	84	70%
0.52-0.63	8	6.66%
<b>Total = 120</b>	<b>120</b>	<b>100%</b>

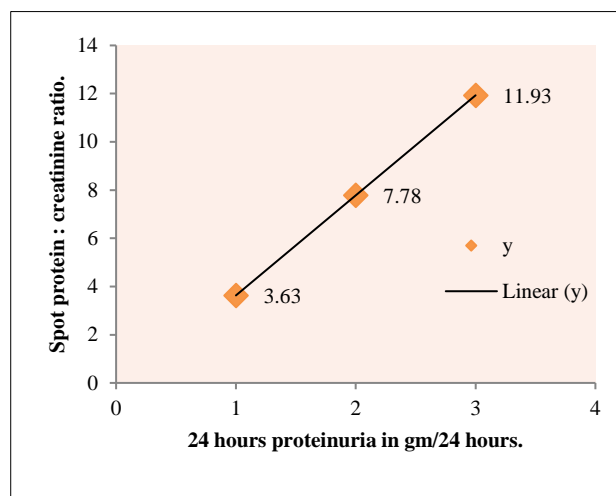
Table 2 shows, among the 120 patients in the study population, 24 patients had a protein: creatinine ratio in the range of 0.12-0.2, 84 had a ratio between 0.25-0.43, while only 8 had a ratio in the range of 0.52-0.63.

Correlation between protein: creatinine ratio in spot sample and 24 hours urinary protein excretion in gm/24 hours in pre eclamptic patients. After applying student “t” test the linear correlation coefficient between the protein: creatinine ratio and 24 hours urine protein excretion was found highly significant ( $r = 0.98$ ,  $p = <0.0001$ ) ( $t$  at 4 df = 9.877084) (Figure 1).

**Table 3: Distribution of patients showing correlation between P/C ratio and 24 hours urine protein excretion.**

Number of cases	24 hours proteinuria (gm/24 hours)	Spot P/C ratio
24	<0.3	0.12-0.2
4	0.3	0.25
84	0.3-1.5	0.25-0.43
8	1.6-2	1.6-2

The linear correlation coefficient between the protein: creatinine ratio and 24 hours urine protein excretion were found highly significant ( $r = 0.98$ ,  $p < 0.0001$ ) (“t” at 4 df = 9.877084).



**Figure 1: XY data: correlation of data file.**

**Table 4: Comparison of 24 hours urine protein to protein: creatinine ratio in a single voided urine sample (n = 120).**

Type	Number of cases	24 hours proteinuria gm/24 hours ( $\geq 0.3$ )	Number of cases	Spot P/C ratio ( $\geq 0.3$ )
Preeclampsia	96	$\geq 0.3$	76	$\geq 0.3$
Pregnancy with hypertension	24	<0.3	44	<0.3
<b>Total = 120</b>	<b>120</b>		<b>Total = 120</b>	

Table 4 shows that out of 120 pregnant women with hypertension, 96 had a 24 hours urine protein excretion  $\geq 0.3$  gm/24 hours. Among them protein: creatinine ratio was positive in (cut off value- 0.3) 76 patients, which were true positive subjects in the study while the 20 subjects had a negative protein: creatinine ratio were the false negative subjects. 44 patients had a protein: creatinine ratio  $< 0.3$ . Out of them 24 hours urine protein excretion  $< 0.3$  gm/24 hours in 24 patients who were true negative subjects and 20 had a positive protein: creatinine ratio who were the false positive study subjects. So, protein: creatinine ratio had a sensitivity of 79% and

specificity of 54%. Thus, it can be said that protein: creatinine ratio is able to correctly identify 76 out of 96 patients with significant proteinuria when the comparison is made with the gold standard test that is 24 hours urine protein.

Table 5 shows that out of 120 pregnant patients with hypertension, 96 had a 24 hours urine protein excretion  $\geq 0.3$  gm/24 hours, which is correlated with protein: creatinine ratio of  $\geq 0.25$ . So, if cut-off value of protein: creatinine ratio is 0.25, diagnosed 96 patients out of 120 patients as pre-eclampsia and rest 24 were diagnosed as

pregnancy with hypertension. So, if take cut off value for protein: creatinine ratio is taken in random urine sample 0.25 or more then sensitivity and specificity become same as 24 hours urine protein.

**Table 5: Comparison of protein creatinine ratio in a single voided urine sample to 24 hours urine protein in study subjects (n = 120).**

Number of cases	24 hours urine protein in gm/24 hours	Spot protein: creatinine ratio
96	≥0.3	≥0.25
24	<0.3	<0.25

## DISCUSSION

Out of the 120 patients included in the study 96 patients had proteinuria more than or equal to 0.3 gm/24 hours. As shown in (Table 1) majority of patients had proteinuria in the range of 0.3-1.5 gm/day. And it is evident from Table 2 that majority of patients had a P/C ratio in the range of 0.25-0.43 and only 4 patients had a P/C ratio of 0.25. The mean urinary protein excretion in 24 hours urine collections was 0.8365±0.50 gm/24 hours (range, 0.2-1.96 gm/24 hours). The mean P/C ratio was 0.3226±0.10 (range, 0.12-0.63).

Several investigators have explored other means of quantifying proteinuria in a shorter period. In this study a comparison of the protein: creatinine ratio with the standard 24 hours protein estimation using the various indices of validity was quite revealing. Sensitivity, specificity. Table 3 shows correlation of 24 hours urine protein and protein: creatinine ratio. The linear correlation coefficient between the protein: creatinine ratio and 24 hours urine protein excretion was found highly significant ( $r = 0.98$ ,  $p < 0.0001$ ) ( $t$  at 4 df = 9.877084), which is comparable to Shahbaazian N et al, study.<sup>6</sup> They found the strong correlation between the spot P/C ratio and 24 hours urine protein excretion ( $r=0.84$ ,  $p < 0.001$ ). The optimal spot P/C ratio cut off point was 0.2 for 300 mg/24 hours of protein excretion with sensitivity 91.2%, specificity 87.8%.

Table 4 shows out of 120 patients pregnancy with hypertension, 96 patients had a 24 hours urine protein excretion greater than or equal to 300 mg. Among 96 patients the P/C ratio was positive (cut off value- 0.3) in 76 patients, which signifies that these were the true positive subjects in the study while the 20 study subjects who had a negative P/C ratio were the false negative subjects. 44 cases of pregnancy with hypertension had P/C ratio <0.3. Out of them 24 hours urine protein excretion <300 mg in 24 patients who were true negative study subjects and 20 had a positive P/C ratio that is they were the false positive study subjects. So, P/C ratio had a sensitivity of 79% and specificity of 54%. Thus, we can say that P/C ratio is able to correctly identify 76 out of 96 patients with significant proteinuria when the comparison is made with the gold standard test that is 24 hours urine

protein. In similar study done by Hossain et al, they found that urine P/C ratio had a sensitivity of 91.67% and the specificity 80% and ( $p$  value is  $< 0.0000001$ ) for discriminating insignificant and significant proteinuria.<sup>7</sup> Based on the above findings they concluded that a random urine protein excretion predicts the amount of 24 hours urine protein excretion with high accuracy.

Table 5 shows it is clear that if cut off value is taken for urine P/C ratio in random urine sample 0.25 or more then sensitivity and specificity become same as 24 hours urine protein. Similar study done by Majid S et al, among 551 pre-eclamptic patients and concludes that urine P/C ratio has shown a high sensitivity, specificity and diagnostic accuracy (at a cut off value of  $> 0.3$ ).<sup>8</sup> So it can be considered a reliable investigation among pre eclamptic patients. The spot urine P/C ratio can provide excellent discrimination between patients with and without significant proteinuria. This test can be used for prompt clinical decision in spite of waiting for 24 hours urine collection. In a similar study done by Aggarwal et al, in 120 pre eclamptic women, the mean age was 26 years and mean gestational age was 32 weeks.<sup>9</sup> They reported a significant association between the two tests with a correlation coefficient of  $r = 0.596$  ( $p < 0.01$ ) and the sensitivity and specificity of spot P/C ratio at a cut off value. 1.14 of 72% and 75%, respectively. But they observed that the values of the spot urine P/C correlated well at higher levels of proteinuria. Thus, they concluded that the test could not rule out mild pre-eclampsia and hence should not be used to replace 24 hours urine protein estimation. Nischintha, Pallavee P, Ghose S et al, found a moderate correlation between 24 hours urine protein and spot urine P/C ratio which was statistically significant ( $r = 0.373$ ,  $p < 0.001$ ).<sup>10</sup> The optimal cut-off value of spot urine P/C ratio for significant proteinuria was  $> 0.6$  at which the sensitivity was 73.53% and specificity was 65.85%.

## CONCLUSION

By this study we concluded that protein: creatinine ratio in a random urine sample is better than random urine protein detection by dipstick method in cases of emergency when there is no time for detection of 24 hours urine protein.

- Sensitivity and specificity of 24 hours urine protein is best but this collection method is cumbersome and not possible in emergency, when there is no time.
- If cut-off level for urine protein: creatinine ratio in random urine sample is taken as 0.25 or more then sensitivity and specificity become same as 24 hours urine protein.

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

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