

Random Urine Protein Creatinine Ratio as a Preadmission Test in Hypertensive Pregnancies with Urinary Protein Creatinine Ratio

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Abstract- To evaluate the value of random urinary protein creatinine ratio in prediction of 24h proteinuria in hypertensive pregnancies. Method: Random urine samples and routine 24h urine collections were collected from hypertensive pregnant women (n=100). Reliability of random urinary protein-creatinine ratio was assessed by receiver operator characteristic (ROC) curve to detect significant proteinuria (≥ 300 mg/day) using 24h. Urine protein as a gold standard. Forty six patients (46%) had significant proteinuria. The random protein creatinine ratio was correlated to 24h urine protein excretion ($r^2=0.777$, $P<0.001$) Area under ROC curve to predict proteinuria was 0.926 (95% CI: 0.854–0.995, $P<0.001$). A cut off value of 0.22mg/mg for protein creatinine ratio best predicted significant proteinuria with sensitivity, specificity, positive and negative predictive values of 87%, 92.6%, 90.6% and 89.3% respectively. Random urinary protein creatinine ratio is a simple inexpensive and excellent alternative to 24h urine collection. It's helpful in diagnosis of preeclampsia and can be used as a pre admission test in PIH cases.

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Introduction

Hypertensive disorders of pregnancy complicates 2-8% of pregnancies and account for maternal and perinatal morbidity and mortality (1,2). The gold standard test to detect and quantify proteinuria which assess the severity of disease is 24h urine collection but it is time consuming, cumbersome and inconvenient (3, 4) 24h urine could be collected in less than half of women admitted for preeclampsia because of delivery.

Routine simple dipstick urinalysis has low sensitivity, high false positive and negative results (5, 6). Random urine protein creatinine ratio could be an alternative to detect significant proteinuria (≥ 300 mg/dl). Urinary creatinine excretion is constant when the glomerular filtration rate is stable, therefore it could be useful reference(7). This method has been a useful for assessing proteinuria in non pregnant population (8, 9).

Several studies have reported a correlation between 24h urine protein and random urine protein – creatinine ratio (8, 10-20) some shows a strong and others a poor correlation (19). The aim of this study was to determine whether we can perform random urine protein creatinine

ratio to rule out significant proteinuria (≥ 300 mg/dl) and to use it as a pre admission test in suspected cases of preeclampsia.

Patients and Methods

All pregnant women with new onset hypertension $\geq 140/90$ mmHg after 20 weeks of gestation were admitted to the department of obstetrics and gynecology, Shariati University Hospital (a tertiary center, in Tehran, Iran) during the time period of October 2007 until January 2009. All these patients were on moderate bed rest and were recommended to have a left lateral decubitus position when in bed. They were allowed to spend a few hours out of bed.

Exclusion criteria included: 1- Women suspicious of having urinary tract infection, 2- Chronic hypertension before pregnancy or in the first half of pregnancy, 3- Preexisting renal disease with proteinuria and 4- Women with diabetic nephropathy.

The study protocol was approved by the Human Ethics Committee and Research Council of Tehran University of medical sciences written informed consent

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Random urine protein creatinine ratio as a preadmission test

was obtained from all patients. Random urine sample for assessing protein-creatinine ratio was obtained after admission, excluding the 1st voided morning urine.

24h urine collection started from 8 AM on the morning following admission. The specimens were sent for protein, creatinine and volume measurement. To assess the adequacy of 24h urine collection the total creatinine of the sample was compared to the predicted creatinine estimated by the Cock Croft Gault equation for women (20). Under collected (<20%) or over collected (>20%) of predicted 24h urine creatinine excretion were discarded. Protein and creatinine measurements were performed within 1h of collection in both.

Urine protein and creatinine were measured by Bio systems (Barcelona, Spain). Statistical analysis was performed with the SPSS version.

The relation ship between the urine proteins: creatinine ratio and 24h proteinuria, were assessed with the Pearson correlation coefficient. Reliability of random urinary protein creatinine ratio was assessed by receiver operator characteristic (ROC) curve to detect significant proteinuria ($\geq 300\text{mg/dl}$) using 24h urine protein as gold standard. The area under curve was calculated and sensitivity, specificity and predictive values of random protein creatinine ratio at various cut-offs for prediction of significant proteinuria were estimated and $P < 0.05$ was considered significant for all analysis. Sample size calculation indicated that a study of 50 subjects was adequate to achieve a high degree of precision in estimating the accuracy of random urinary protein creatinine ratio as a diagnostic test for significant proteinuria.

Results

A total of one hundred thirteen 24h urine specimen were collected and 13 were discarded because of inadequate urine collection. Characteristics of study population are shown in table 1. Pregnancy was terminated in 10 patients because of severe preeclampsia, in one because of placental abruption, and another one because of fatty liver. No patient developed eclampsia. The random protein creatinine ratio (PCR) was strongly correlated to 24h urine protein excretion ($r=0.777$, $P<0.001$) (Figure 1). Area under curve to predict significant proteinuria $>300\text{mg}/24\text{h}$ was 0.926 (95% CI: 0.854-0.995 $P<0.001$). A cut off value of $>0.22\text{mg}/\text{mg}$ for protein creatinine ratio best predicted significant proteinuria with sensitivity of 87.9% specificity of 92.6%, positive and negative predictive values of 90.6% and 89.3% respectively (Figure 2).

Table 1. Characteristics of study population (n=100)

| | |
|---|----------------------------|
| Age (yr) | 30.6 (19-44) |
| Parity | N: 35 (35%) M: 65 (65%) |
| GA ^w | 31 (22 – 39) |
| BP (mmHg) | 145 (120-180) |
| Systolic | |
| Diastolic | 91.9 (90-110) |
| Protein creatinine ratio (mg/mg) | 0.22 (0.006-5.1) |
| 24h urine protein (mg) | 268.5 (15-3520) |
| Significant proteinuria $\geq 300\text{mg/d}$ | 46 (46%) |
| Proteinuria $>2000\text{mg/d}$ | 4 (4%) |

N: Nullipara, M: Multipara, GA: Gestational Age, BP: Blood pressure

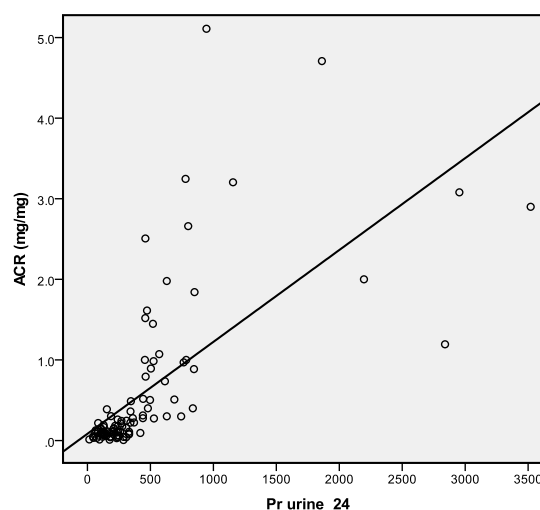


Figure 1. The ACR in the random urine sample is correlated to the total 24h urine protein

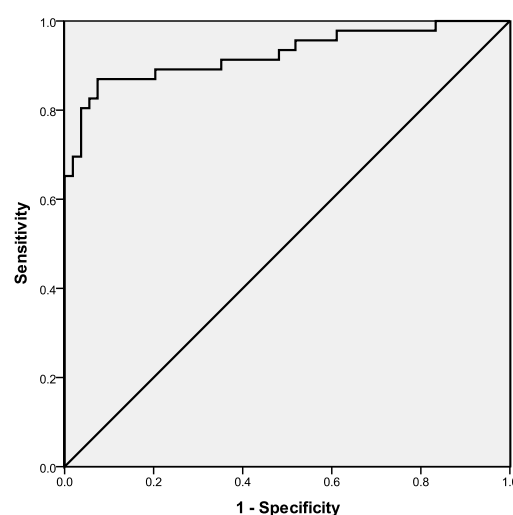


Figure 2. ROC curve showing the performance of random urine ACR for significant proteinuria

Fifty (42.6%) of the 54 patients who had not significant proteinuria, had PCR less than 0.22mg/mg. All of 18 (100%) patients with severe preeclampsia had PCR more than 0.22mg/mg. Twenty-Two (78.4%) of 28 patients with mild preeclampsia had PCR >0.22mg/mg and 6 (21.6%) had PCR <0.22mg/mg.

Discussion

To establish the diagnosis of preeclampsia and its severity, measurement of proteinuria is mandatory. Using random urine sample is more convenient than 24h urine collection for screening proteinuria. Sure patient compliance is better. It's both faster and simpler. There is no problem with inadequate collection (21, 22) specially when there is no enough time to collect 24h urine in severe hypertension since delivery is planned, (3, 4) or in mild cases intervention would be less.

The study shows random urinary protein creatinine ratio measurement is valuable in predicting 24h urine protein in hypertensive pregnant women. There was a good correlation between random urine protein – creatinine ratio (PCR) and total urine protein in 24h urine collection. Justessen, Nisell and Leonos – Miranda reported a significant correlation ($r=0.98$, 0.8 respectively) (8,14-15), Zadeh Modarres *et al.* found a good correlation(16), while Wilkström reported a poor correlation ($r=0.4$), but again there was a good correlation when adjustment was performed for age ($r^2 = 0.60$) (19). There fore he has proposed to use PCR of a 24h urine collection because of its significant correlation with a 24h total urine protein. Yet there will be the previous problem of 24h urine collection.

The ROC curve analysis showed an area under the curve of 0.926 (95 CI: 0.854–0.995), indicating that PCR is adequate to detect or rule out significant proteinuria.

The cut-off value that best predicted significant proteinuria of a random PCR was 0.22mg/mg since this cut – off yields a high diagnostic performance with a sensitivity of 87% and specificity of 92.6% and high positive and negative predictive values of 90.6% and 89.3% respectively. 100% of patients with severe preeclampsia had a PCR > 0.22mg/mg and 92.6% of patients who had not significant proteinuria had a PCR <0.22mg/mg.

Several cut-off and different units have been reported for PCR value in different reported studies (12). Some reported optimal cut-off points (0.15-0.5mg/mg) are similar to this study (12) and yield sensitivities and

specificities of 83% (77.5-89.7%) and 76.3% (72.6% to 80%) respectively. The sensitivity and specificity of the present study is higher.

There was a high incidence of significant proteinuria in this study. It could be due to: 1st Shariati Hospital is referral center, 2nd the patients examined had high blood pressures and were expected to have proteinuria.

There are some limitations in this study. First the patients were all hospitalized during urine collection, although they were allowed to walk around. Second the cases which had >1g proteinuria was small.

The study shows a good correlation between random urine PCR and 24h urine total protein despite wide confidence intervals for a wide range of proteinuria. It can be recommended to use random urine PCR in screening significant proteinuria in suspected cases of preeclampsia. The random urine PCR of 0.22mg/mg reliably predicts 24h urine total protein of ≥ 300 mg/dl.

In Conclusion: Random urinary protein creatinine ratio is a simple inexpensive and excellent alternative to 24h urine collection. It's helpful in diagnosis of preeclampsia and can be used as a preadmission test in PIH cases.

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Random urine protein creatinine ratio as a preadmission test

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