Correlation between Random Urinary Protein-to-Creatinine Ratio and Quantitation of 24-hour Proteinuria in Preeclampsia

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Abstract

Objective : To determine whether random urinary protein-to-creatinine ratio correlated with the quantitation of 24-hour proteinuria in cases of preeclampsia.

Design : Cross-sectional descriptive study.

Subjects : Pregnant patients hospitalized in the obstetric ward, King Chulalongkorn Memorial Hospital due to preeclampsia.

Method : The random urine specimens were obtained from the eligible subjects for protein-to-creatinine ratio determination, the subjects were then instructed to collect 24-hour urine samples for protein measurement.

Results : Twenty-five pregnant patients completed the study. There was a strong correlation between the random urinary protein-to-creatinine ratio and the quantitation of 24-hour proteinuria ($r = 0.929$, $p < 0.001$).

Conclusion : The presented data support a strong correlation between random urinary protein-to-creatinine ratio and quantitation of 24-hour proteinuria in hospitalized pregnant patients with preeclampsia.

Key word : Urinary Protein-to-Creatinine Ratio, 24-Hour Proteinuria, Preeclampsia

YAMASMIT W, WONGKITISOPHON K,
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J Med Assoc Thai 2003; 86: 69-73

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Hypertensive disorders complicating pregnancy are common and form one of the deadly triads, along with hemorrhage and infection, that result in much of the maternal morbidity and mortality related to pregnancy[1]. It is clear that when blood pressure begins to rise, both mother and fetus are at increased risk[2]. Proteinuria is a sign of worsening hypertensive disease, specifically preeclampsia; and when it is overt and persistent, maternal and fetal risks are increased even more[3].

Preeclampsia is a pregnancy-specific syndrome of reduced organ perfusion secondary to vasospasm and endothelial activation. Proteinuria is an important sign of preeclampsia and is described as 300 mg or more of urinary protein per 24 hours[4]. The 24-hour urine collection for protein measurement has been the gold standard for making the diagnosis of significant proteinuria in cases of preeclampsia. The test is cumbersome and takes 24 hours to complete. This leads to a delay in diagnosis of preeclampsia and an inaccurate result due to incomplete collection of the specimen[5,6]. A rapid and reliable method for diagnosing significant proteinuria is needed in assisting clinicians in making more timely decisions regarding delivery and in using magnesium for seizure prophylaxis. The dipstick has been shown to be inaccurate and had low sensitivity compared with the 24-hour urine collection[7]. The use of random urinary protein-to-creatinine ratio to assess proteinuria in a nonpregnant population has been substantiated in the literature[8,9]. Several previous studies showed a strong linear association between the random urinary protein-to-creatinine ratio and the 24-hour urine protein in healthy and hypertensive pregnant women. Correlation coefficients reported ranges as high as 0.928 to 0.995[5,10-12]. To the authors' knowledge, there is no such report in pregnant Thai women. This study was conducted to evaluate whether random urinary protein-to-creatinine ratio correlated with the quantitation of 24-hour proteinuria in pregnant women complicated with preeclampsia in King Chulalongkorn Memorial Hospital.

MATERIAL AND METHOD

The study was approved by The Ethics Committee of the Faculty of Medicine, Chulalongkorn University. Thirty-two women who were diagnosed as preeclampsia and admitted to the obstetric ward, King Chulalongkorn Memorial Hospital were recruited. The definition of preeclampsia in the present study included the condition of superimposed preeclampsia on chronic hypertension. Preeclampsia was diagnosed when a pregnant woman had blood pressure $\geq$ 140/90 mmHg after 20 weeks'gestation and had urine protein $\geq$ 1+ by dipstick[13]. The pregnant women who had chronic hypertension without proteinuria before 20 weeks'gestation and had new-onset urine protein $\geq$ 1+ by dipstick were diagnosed as superimposed preeclampsia[13].

To participate in the study, the patients had to give written informed consent. They all had neither underlying primary/secondary renal disease nor urinary tract infection. The eligible subjects were asked to collect random urine (except first void morning urine) for protein-to-creatinine ratio determination. Then they were instructed to collect urine for 24 hours. The subjects who could not collect complete 24-hour urine were excluded. Urine protein level was measured by the dye-binding colorimetric method which utilized pyrogallol red-molybdate complex, and urine creatinine level was determined by the Jaffe rate method. All tests were done on the Beckman Synchron CX3 System (Beckman Instruments, USA) by laboratory service of the Nephrology Unit, Department of Medicine, Faculty of Medicine, Chulalongkorn University.

The authors selected a sample size of 25 which is enough to detect correlation with a correlation coefficient of more than or equal to 0.6 at the 0.05 significance level and a power of 90 per cent [14]. Statistical analysis were performed with the SPSS statistical package version 10.0. Descriptive statistics were used for demographic and baseline data and summarized as mean/median or per cent. To evaluate the correlation between a random urinary protein-to-creatinine ratio and a quantitation of 24-hour proteinuria, a simple linear regression with calculation of a Pearson correlation coefficient was used. p-value less than 0.05 was considered as statistical significance.

RESULTS

Thirty-two pregnant patients were recruited. Seven patients initially enrolled were excluded in the final analysis. Of these 7 patients, 5 patients were delivered before the completion of the 24-hour urine collection, 1 patient had urinary tract infection and the other had adult polycystic kidney disease with

chronic renal failure, leaving twenty-five patients for the analysis.

The maternal age ranged from 18 to 39 years (mean ± SD = 30.1 ± 5.43 years). The gestational age at recruitment ranged from 26 to 40 weeks (mean ± SD = 35.5 ± 3.28 weeks). Ninety-six per cent (24/25) of the patients were in the third trimester and only 4 per cent (1/25) in the second trimester. Sixteen patients (64%) were nulliparous. Twenty-three patients had singleton and two patients had twin pregnancies. Most of patients in the present study (21/25) were diagnosed as mild preeclampsia, 2 patients had severe preeclampsia and 2 patients had superimposed preeclampsia.

The median 24-hour urine protein excretion was 493 mg (range from 70 to 5,560 mg), and the median random urine protein-to-creatinine ratio was 0.45 (range from 0.07 to 6.56). Sixty-eight per cent (17/25) of the study population had significant proteinuria as determined by the 24-hour urine collection and 12 per cent (3/25) had a 24-hour urine protein excretion of > 2 g per 24 hours.

Fig. 1 graphically displays the relationship of the random urinary protein-to-creatinine ratio and 24-hour proteinuria. There was a high degree of correlation, with a Pearson correlation coefficient of 0.929 ($p < 0.001$).

DISCUSSION

This study demonstrated a strong correlation between random urinary protein-to-creatinine ratio and the quantitation of 24-hour proteinuria in pregnant women complicated with preeclampsia. It supported the results of previous studies although those studies were conducted in a different population and using different methods. Boler et al[11]. reported excellent correlation (r = 0.994) with these two methods, however, their study included both ambulatory normotensive and hypertensive pregnant women. Jaschevatzky et al[10] in Israel also found good correlation (r = 0.928) in preeclamptic pregnant women, but they used random urine in the morning after complete collection of 24 hours urine. Robert et al[5] used random urine collected during the 24-

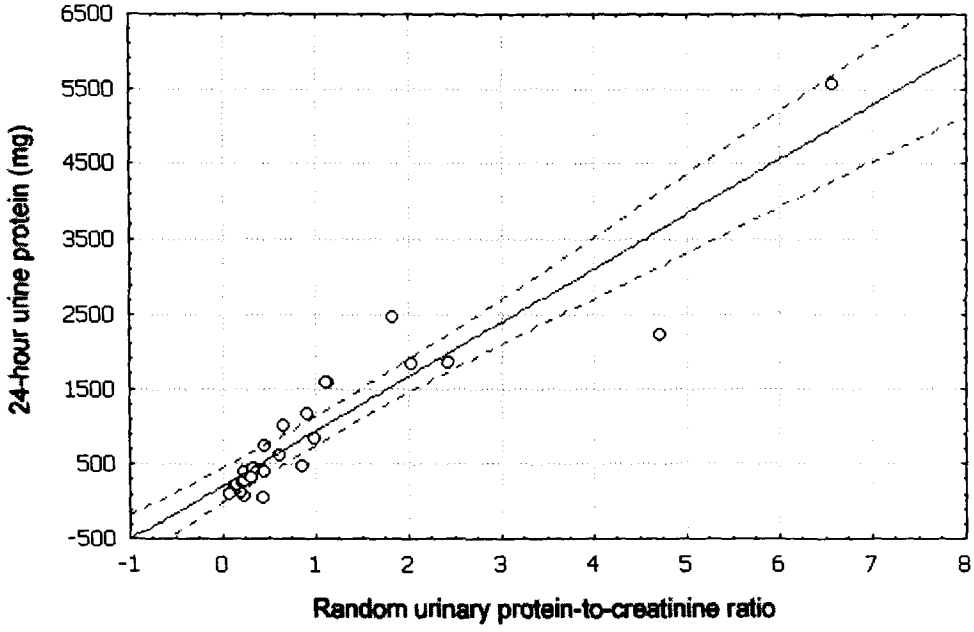

Fig. 1. Correlation between 24-hour protein excretion and the random urinary protein-to-creatinine ratio. Each *circle* represents 1 patient. The solid line indicates the regression (24-hour protein = 723.9 x [urinary protein-to-creatinine ratio] + 221.6; r = 0.929; p < 0.001); the broken line indicates the 95% CI.

hour urine collections and found a strong correlation with a correlation coefficient of 0.94 in Canadian patients. In the present study, the authors chose to evaluate the random urine samples that were collected before the 24-hour urine because the results of a random urine specimen could be altered if patients remained at bed rest during the collecting period. In addition, it most closely resembles how the test would be used in practice if the correlation is shown. However, the random urine samples in the present study were never obtained from the first voided morning specimen because protein excretion is affected by postural change, being less after prolonged supine position or bed rest.

In preeclamptic patients with a 24-hour protein excretion over 2 g, Jaschevatzky et al(10) reported a significant ($p < 0.05$) but lower degree of correlation between random urinary protein-to-creatinine ratio and 24-hour proteinuria. Since most of the presented study population were diagnosed as mild preeclampsia, the prevalence of 24-hour protein excretion over 2 g ($n = 3$) was not high enough to perform a subgroup analysis.

Because protein excretion is greater in the upright position than in the supine position, it is important to know the ambulatory status of the subject. The presented study population was hospitalized preeclamptic patients, therefore, the results could not be extrapolated to other patient's conditions or an ambulatory population.

Because random urinary protein-to-creatinine ratio is easily collected and the results can be obtained promptly, it seems promising to use the random urinary protein-to-creatinine ratio for diagnosis of significant proteinuria in clinical practice. Nevertheless, it needs a further larger study to determine the best cutoff point.

(Received for publication on October 3, 2002)

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ความสัมพันธ์ระหว่างอัตราส่วนโปรตีนต่อครีอาทินีนในปัสสาวะที่เก็บแบบสุ่มและปริมาณโปรตีนในปัสสาวะที่เก็บ 24 ชั่วโมงในสตรีภาวะครรภ์เป็นพิษ

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วัตถุประสงค์ : เพื่อประเมินความสัมพันธ์ระหว่างอัตราส่วนโปรตีนต่อครีอาทินีนในปัสสาวะที่เก็บแบบสุ่มและปริมาณโปรตีนในปัสสาวะที่เก็บ 24 ชั่วโมงในสตรีภาวะครรภ์เป็นพิษ

รูปแบบการศึกษา : การศึกษาเชิงพรรณนา แบบตัดขวาง

ประชากรกลุ่มตัวอย่าง : สตรีตั้งครรภ์ที่เข้ารับการรักษาตัวในหอผู้ป่วยสูติกรรม โรงพยาบาลจุฬาลงกรณ์ เนื่องจากครรภ์เป็นพิษ

วิธีการศึกษา : เก็บปัสสาวะแบบสุ่มจากผู้ป่วยที่ได้รับการคัดเลือก เพื่อนำไปประเมินอัตราส่วนโปรตีนต่อครีอาทินีน จากนั้นให้คำแนะนำผู้ป่วยดังกล่าวในการเก็บปัสสาวะ 24 ชั่วโมงเพื่อตรวจวัดปริมาณโปรตีน

ผลการศึกษา : มีสตรีภาวะครรภ์เป็นพิษทั้งหมด 25 ราย ที่มีคุณสมบัติครบถ้วนตามหลักเกณฑ์ที่กำหนด และพบว่าอัตราส่วนโปรตีนต่อครีอาทินีนในปัสสาวะที่เก็บแบบสุ่มมีความสัมพันธ์อย่างสูงมากกับปริมาณโปรตีนในปัสสาวะที่เก็บ 24 ชั่วโมง ($r = 0.929$, $p < 0.001$)

สรุป : ผลการศึกษานี้สนับสนุนข้อมูลที่แสดงถึงความสัมพันธ์ที่สูงมากระหว่างอัตราส่วนโปรตีนต่อครีอาทินีนในปัสสาวะที่เก็บแบบสุ่มและปริมาณโปรตีนในปัสสาวะที่เก็บ 24 ชั่วโมงในสตรีตั้งครรภ์ที่เข้ารับการรักษาตัวในโรงพยาบาลเนื่องจากครรภ์เป็นพิษ

คำสำคัญ : อัตราส่วนโปรตีนต่อครีอาทินีนในปัสสาวะ, โปรตีนในปัสสาวะ 24 ชั่วโมง, ภาวะครรภ์เป็นพิษ

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จดหมายเหตุทางแพทย์ ฯ 2546; 86: 69–73

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