Correlation of 4- and 24-hour Urine Protein in Women with Initially Diagnosed Hypertensive Disorders in Pregnancy

KITTI WONGKITISOPHON, MD*,
WARALAK YAMASMIT, MD*,
YUEN TANNIRANDORN, MD*,
VORAPONG PHUPONG, MD*,
PONGSAK PANSIN, BSc**,
DHIRAPHONGS CHAROENVIDHYA, MD*

Abstract

Objective : To determine whether 4-hour urine protein value correlates with 24-hour urine protein value in women with hypertensive disorders in pregnancy.

Study design: Cross-sectional study was performed in 38 in-patient pregnant women who were initially diagnosed as having hypertensive disorders in pregnancy. Urine samples were collected within 24 hours in 2 successive periods: the first 4-hour and the next 20-hour urine, in separate containers. The urine volume, urine protein and creatinine concentrations were thus separately measured. The 4- and 24-hour urine proteins were calculated and the correlation between both groups was determined by simple linear regression analysis.

Results : A total of 38 patients were recruited into the study, 26 had mild preeclampsia, 5 had severe preeclampsia, and 7 had superimposed preeclampsia. The result of the 4-hour urine protein was found to correlate with those of the 24-hour urine protein for patients with hypertensive disorders in pregnancy ($p < 0.001$).

Conclusion : Total protein values of 4-hour samples positively correlated with values of 24-hour samples of patients with hypertensive disorders in pregnancy. This might be modified and used for urine protein collection in outpatients to improve the compliance.

Key word : Preeclampsia, Superimposed Preeclampsia, Proteinuria, 4-hour Urine, 24-hour Urine

WONGKITISOPHON K, PHUPONG V, YAMASMIT W, PANSIN P, TANNIRANDORN Y, CHAROENVIDHYA D
J Med Assoc Thai 2003; 86: 529-534

* Department of Obstetrics and Gynecology,
** Research Laboratory of Nephrology Unit, Department of Medicine,Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.

Hypertensive disorders in pregnancy are classified into five groups. These include gestational hypertension, preeclampsia, eclampsia, superimposed preeclampsia and chronic hypertension[1]. Nevertheless, such diseases with proteinuria have been classified into 3 types: preeclampsia, eclampsia, and superimposed preeclampsia. In this regard, the level of protein in urine plays an important role in the diagnosis of these diseases.

The incidence of preeclampsia is 4-8 per cent of pregnancies[2,3]. It is categorized as mild and severe preeclampsia. Mild preeclampsia is defined as the presence of blood pressure ≥ 140/90 mmHg and preoteinuria ≥ 300 mg/24 hours or ≥ 1+ dipstick in over 20 weeks' gestation[1]. Severe preeclampsia is defined as having one or more of the following criteria: blood pressure of at least 160/110 mmHg measured on two occasions of 6 hours apart, proteinuria of at least 2 g per 24 hours, or at least 2+ on dipstick testing, oliguria of less than 500 ml per 24 hours, cerebral or visual disturbances, pulmonary edema or cyanosis, epigastric or right upper quadrant pain, impaired liver function, thrombocytopenia, fetal growth restriction[1]. Eclampsia is the occurrence of seizures in a woman with preeclampsia that cannot be attributed to other causes[1]. Its incidence has ranged from 0.01 per cent to 0.68 per cent[2,4,5].

Superimposed preeclampsia upon chronic hypertension in the present study was determined by evidence of new onset proteinuria ≥ 300 mg/24 hours or ≥ 1+ dipstick in hypertensive women but no proteinuria before 20 weeks' gestation[1].

The gold standard method of measurement of accurate proteinuria is 24-hour collection of urine protein[1], which has been in use for a long time. The problem of this 24-hour urine protein collection is that it requires too much time to collect. The results are usually too late for the treatment of preeclampsia. So several investigators have previously reported more rapid methods to identify proteinuria such as the use of dipsticks for protein and protein-creatinine ratios in random urine specimens. These methods have not been shown to correlate with the severity of the disease as determined by the results of 24-hour urine collection[6-11].

The objective of this study was to determine whether 4-hour urine protein samples have any correlation with 24-hour urine protein samples. The studied population was limited to pregnant women initially diagnosed as hypertensive disorders in pregnancy, excluding eclampsia, because of the total time of urine collection consuming over 24 hours. Therefore, it would not be safe for patients with eclampsia, who needed immediate care, thus they were not recruited into the study.

MATERIAL AND METHOD

The study was done from June, 2002 to December, 2002. All pregnant women, who were > 20 weeks' gestation with diastolic blood pressure ≥ 90 mmHg and a urine dipstick for protein ≥ 1+ at antenatal clinic, as initially diagnosed preeclampsia, or who had new onset proteinuria ≥ 1+ in hypertensive women but without proteinuria before 20 weeks' gestation, as initially diagnosed superimposed preeclampsia were admitted for further investigation and treatment in the obstetric ward. They all were counseled about the disease and method to confirm their diagnosis. The 4-hour and 20-hour urine collection methods were explained to the patients who accepted and signed their consent forms. The study was approved by the Ethics Committee of the Faculty of Medicine. Patients who had renal diseases or did not complete their 24-hour urine collection due to delivery or discharge were excluded from the study.

The urine was collected in 2 separate, clearly marked, different-color labeled containers. The first yellow-labeled container was for the first 4-hour urine collection and the second pink-labeled container was for the remaining 20-hour urine collection. At the beginning of the collection, urine must be voided before beginning collection. Each container was marked with the patient's running number, and the collection time.

The urine protein and the urine creatinine values were measured by a well-trained technician at the Research Laboratory of Nephrology Unit, Department of Medicine, Faculty of Medicine, Chulalongkorn University. After urine was stirred, the urine protein concentrations (mg/dl) were measured by the modified dye-binding colorimetric method utilizing pyrogallol red-molybdate complex[12]. The urine protein weight (mg) was calculated by urine protein concentration multiplied with urine volume of each specimen. The total 24-hour urine protein weight (mg) was calculated by 4-hour urine protein (mg) plus 20-hour urine protein (mg). The urine creatinine was measured by using a modified Jaffe reaction[13].

The sample size that was calculated from the prior pilot study equaled 38 patients. The data were analyzed with the SPSS software package version 10.0 for Windows (SPSS Inc, Chicago, USA) and

expressed in terms of mean, standard deviation, and percentage. The results of the 4-hour urine samples were compared to the 24-hour urine results by simple regression analysis to determine a correlation coefficient (r) by using SPSS version 10.0. A p-value of < 0.05 was considered statistically significant.

RESULTS

A total number of 38 patients were recruited into the study, 26 had mild preeclampsia, 5 had severe preeclampsia, and 7 had superimposed preeclampsia. Table 1 shows the demographic data of the patients. Demographic data for patients in each of the three groups is shown in Table 2. There was a strong correlation between 4- and 24-hour urine protein ($r = 0.955$, $p < 0.001$). The regression equation was $Y = 4.02X + 171.386$ ($p < 0.001$) (Fig. 1).

Random urine dipstick results are shown in Table 3.

Table 1. Characteristics of all patients.

	All patients (n = 38)
Mean age (years)	30.7 ± 5.7
Mean gestational age (days)	243.5 ± 24.1
Mean BW (kg)	75.3 ± 13.5
Mean height (cm)	155.6 ± 4.9
Systolic blood pressure (mmHg)	147.4 ± 11.1
Diastolic blood pressure (mmHg)	96.3 ± 10.0
Primigravida (%)	26.3
Singleton (%)	92.1
Twins (%)	7.9

DISCUSSION

The result of the present study revealed that the 4-hour urine protein level strongly correlated with the 24-hour urine protein level in pregnant women who were initially diagnosed with hypertensive disorders in pregnancy.

Many investigators have used other methods of quantifying proteinuria in a shorter time[6-11]. Firstly, random urine dipstick for protein, a very simple and cheap method, plays a role as the first investigation with the significant value ≥ 1+ in preeclampsia[14]. Nevertheless, its value seems to be inaccurate to diagnose preeclampsia as shown that 64-66 per cent of the patients with negative or trace protein had significant proteinuria[6]. The present study also confirmed that urine dipstick results do have good correlation with the 24-hour sample.

Secondly, random urine protein-creatinine ratio has been proved in several studies to have strong correlation with 24-hour urine protein in preeclampsia [8-11]. However, in patients with 24-hour protein excretion over 2 grams, the degree of correlation was lower. So it must be considered in patients with marked proteinuria[11]. The protein-creatinine ratio of random urine in preeclampsia has been shown to correlate significantly with protein values[8-11]. One study was shown to correlate only with protein values of < 2 grams in 24 hours. Above this level the variation between the samples increases[11].

Recently, studies with a shorter time of collection such as 8-hour or 12-hour have shown that they have correlation with 24-hour urine samples in preeclampsia. However, it takes too long for the diagnosis of preeclampsia[7].

The present study used a shorter time (4-hour) than the previous study[7], and found a strong

Table 2. Characteristics of categorized patients.

	MPE (n = 26)	SPE (n = 5)	SIPE (n = 7)
Mean age (years)	29.2 ± 5.8	32.0 ± 5.2	35.1 ± 3.1
Mean gestational age (days)	249.2 ± 21.8	226.4 ± 25.5	234.9 ± 26.2
Mean BW (kg)	78.0 ± 15.0	67.1 ± 3.8	71.2 ± 8.9
Mean height (cm)	156.6 ± 4.8	151.3 ± 4.2	151.1 ± 4.7
Systolic blood pressure (mmHg)	142.7 ± 5.3	166.0 ± 15.2	151.4 ± 9.0
Diastolic blood pressure (mmHg)	93.1 ± 4.7	114.0 ± 16.7	95.7 ± 5.3
Primigravida (%)	30.8	0	28.6
Singleton (%)	88.5	100	100
Twins (%)	11.5	0	0

MPE = mild preeclampsia, SPE = severe preeclampsia, SIPE = superimposed preeclampsia.

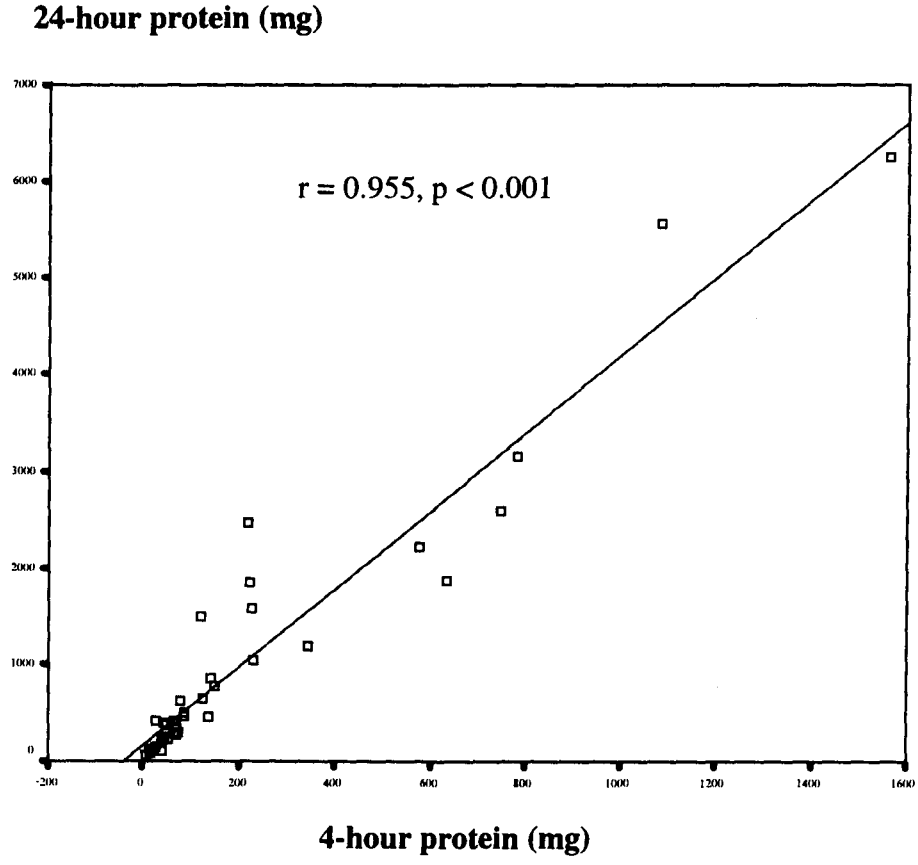

Fig. 1. Correlation between 4-hour protein and 24-hour protein.

Table 3. Urine dipstick results categorized according to 24-hour urine protein results.

Urine dipstick (n = 38)	1+	2+	3+	4+
No proteinuria (n = 13)	11	2	0	0
Mild proteinuria (n = 23)	14	6	2	1
Severe proteinuria (n = 2)	0	0	2	0

No proteinuria : urine protein level < 300 mg/24 h
Mild proteinuria : urine protein level ≥ 300 mg/24 h but less than 5 g/24 h
Severe proteinuria : urine protein level ≥ 5 g/24 h

correlation between 4-hour urine protein and 24-hour urine protein. This might be modified and used for urine collection in outpatients. This will improve the patients' compliance and shorten the time to diagnose hypertensive disorders in pregnancy.

In conclusion, the use of a 4-hour urine specimen method seems more satisfactory for patients than the generally used 24-hour collection method. Compliance and accuracy of the results can be assumed even on an outpatient basis.

ACKNOWLEDGEMENTS

The authors wish to thank Professor Dr. Somchai Eiam-Ong, for his valuable comments on the study. This work was supported by Grant number PP09, Ratchadapiseksompotch Fund, Faculty of Medicine, Chulalongkorn University.

(Received for publication on January 9, 2003)

REFERENCES

1. Cunningham FG, Gant NF, Leveno KJ, Gilstrap LC III, Hauth JC, Wenstrom KD. Williams obstetrics. 21st ed. New York: McGraw-Hill; 2001: 567-618.
2. Obstetric audit; statistical report 1996-2000 A.D. Bangkok: Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University.
3. Norwitz ER, Robinson JN, Repke JT. Prevention of preeclampsia: Is it possible? Clin Obstet Gynecol 1999; 42: 436-54.
4. Moller B, Lindmark G. Eclampsia in Sweden, 1976-1980. Acta Obstet Gynecol Scand 1986; 65: 307-14.
5. Ferraz EM, Sherline DM. Convulsive toxemia of pregnancy (eclampsia). South Med J 1976; 69: 152-6.
6. Meyer NL, Mercer BM, Friedman SA, Sibai BM. Urinary dipstick protein: A poor predictor of absent or severe proteinuria. Am J Obstet Gynecol 1994; 170: 137-41.
7. Adelberg AM, Miller J, Doerzbacher M, Lambers DS. Correlation of quantitative protein measurements in 8-, 12-, and 24-hour urine samples for the diagnosis of preeclampsia. Am J Obstet Gynecol 2001; 185: 804-7.
8. Boler L, Zbella EA, Gleicher N. Quantitation of proteinuria in pregnancy by the use of single voided urine samples. Obstet Gynecol 1987; 70: 99-100.
9. Rodriguez-Thompson D, Lieberman ES. Use of a random urinary protein-to-creatinine ratio for the diagnosis of significant proteinuria during pregnancy. Am J Obstet Gynecol 2001; 185: 808-11.
10. Robert M, Sepandj F, Liston RM, Dooley KC. Random protein-creatinine ratio for the quantitation of proteinuria in pregnancy. Obstet Gynecol 1997; 90: 893-5.
11. Jaschevatzky OE, Rosenberg RP, Shalit A, Zonder HB, Grunstein S. Protein/creatinine ratio in random urine specimens for quantitation of proteinuria in preeclampsia. Obstet Gynecol 1990; 75: 604-6.
12. Orsonneau JL, Douet P, Massoubre C, Lustenberger P, Bernard S. An improved pyrogallol red-molybdate method for determining total urinary protein. Clin Chem 1989; 35: 2233-6.
13. Bonsnes RW, Taussky HH. On the colorimetric determination of creatinine by the Jaffe reaction. J Biol Chem 1945; 158: 581-91.
14. Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy. Am J Obstet Gynecol 2000; 183: S1-S22.

การหาความสัมพันธ์ของการตรวจโปรตีนในปัสสาวะ 4 ชั่วโมงและ 24 ชั่วโมงในภาวะครรภ์เป็นพิษและภาวะครรภ์เป็นพิษแทรกซ้อน

กิตติ วงษ์กิติโสภณ, พบ, วรพงศ์ ภู่พงศ์, พ.บ., วราลักษณ์ ยมะสมิต, พบ*, พงษ์ศักดิ์ พันสิน, วทบ (เทคนิคการแพทย์)**, เยื้อน ตันนิรันดร, พบ*, ธีระพงศ์ เจริญวิทย์, พบ**

วัตถุประสงค์ : เพื่อศึกษาหาความสัมพันธ์ระหว่างการตรวจโปรตีนในปัสสาวะ 4 ชั่วโมงและ 24 ชั่วโมงในภาวะครรภ์เป็นพิษและภาวะครรภ์เป็นพิษแทรกซ้อน

การศึกษา : การศึกษาแบบ Cross-sectional ในหญิงตั้งครรภ์ที่มีภาวะครรภ์เป็นพิษและภาวะครรภ์เป็นพิษแทรกซ้อนจำนวน 38 ราย โดยการเก็บปัสสาวะทั้งหมด 24 ชั่วโมง ซึ่งแยกเก็บเป็น 2 ช่วงคือ 4 ชั่วโมงแรกและ 20 ชั่วโมงต่อไป และแยกการตรวจวัดปริมาตรของปัสสาวะ โปรตีนและครีตีนินในปัสสาวะ 4 ชั่วโมงแรกและ 20 ชั่วโมง การคำนวณหาความสัมพันธ์ระหว่างการตรวจโปรตีนในปัสสาวะ 4 ชั่วโมงและ 24 ชั่วโมงนั้นใช้การหาความสัมพันธ์เชิงเส้นตรง (simple linear regression analysis)

ผลการศึกษา : มีหญิงตั้งครรภ์เข้าร่วมในการศึกษาทั้งหมด 38 รายโดยมีภาวะครรภ์เป็นพิษชนิดรุนแรงน้อย 26 ราย มีภาวะครรภ์เป็นพิษชนิดรุนแรงมาก 5 รายและมีภาวะครรภ์เป็นพิษแทรกซ้อนในความดันโลหิตสูง 7 ราย พบว่าการตรวจโปรตีนในปัสสาวะ 4 ชั่วโมงมีความสัมพันธ์กับการตรวจโปรตีนในปัสสาวะ 24 ชั่วโมงในหญิงตั้งครรภ์ที่มีภาวะครรภ์เป็นพิษและภาวะครรภ์เป็นพิษแทรกซ้อนอย่างมีนัยสำคัญทางสถิติ จำนวน ($P < 0.001$)

สรุปผลการศึกษา : การตรวจโปรตีนในปัสสาวะ 4 ชั่วโมงมีความสัมพันธ์กับการตรวจโปรตีนในปัสสาวะ 24 ชั่วโมงในหญิงตั้งครรภ์ที่มีภาวะครรภ์เป็นพิษและภาวะครรภ์เป็นพิษแทรกซ้อน ซึ่งอาจจะนำมาประยุกต์ใช้ในการเก็บปัสสาวะเพื่อตรวจหาโปรตีนในผู้ป่วยนอก จะทำให้ได้รับความร่วมมือดีขึ้น

คำสำคัญ : ภาวะครรภ์เป็นพิษ, ภาวะครรภ์เป็นพิษแทรกซ้อนในความดันโลหิตสูง, โปรตีนในปัสสาวะ, ปัสสาวะ 4 ชั่วโมง, ปัสสาวะ 24 ชั่วโมง

กิตติ วงษ์กิติโสภณ, วรพงศ์ ภู่พงศ์, วราลักษณ์ ยมะสมิต, พงษ์ศักดิ์ พันสิน, เยื้อน ตันนิรันดร, ธีระพงศ์ เจริญวิทย์
จดหมายเหตุทางแพทย์ ฯ 2546; 86: 529-534

* ภาควิชาสูติศาสตร์-นรีเวชวิทยา,

** ห้องปฏิบัติการวิจัย, หน่วยโรคไต, ภาควิชาอายุรศาสตร์, คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย, กรุงเทพฯ 10330