Comparison of 24-hour urinary protein and protein-to-creatinine ratio in women with preeclampsia

Semra Kayatas [a], Emre Erdogdu [a,*], Erbil Cakar [a], Vefa Yılmazer [a], Sevcan Arzu Arınkan [a], Vedat Erkan Dayıcıoglu [b]

[a] Zeynep Kamil Gynecologic and Pediatric Training and Research Hospital, Istanbul, Turkey
[b] Special Office, Istanbul, Turkey

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ABSTRACT

Objective: To compare the spot urine protein-to-creatinine (P/C) ratio and 24-hour urine protein excretion in pregnant women with preeclampsia and also to determine the best discriminator values of the spot P/C ratios for 300 mg and 2000 mg protein per 24 h.

Study design: Prospective study of 200 pregnant women with new onset hypertension at or greater than 140/90 mmHg after 20 weeks of gestation. Women were instructed to collect urine during a 24-hour period, and after the 24-hour urine sample collection was completed a mid-stream urine specimen was obtained for P/C ratio determination. The correlation between 24-hour urine protein excretion and spot urine P/C ratio was calculated. The receiver operating characteristic (ROC) curve was used to identify the cut-off values of the spot P/C ratios for 300 mg and 2000 mg protein per 24 h. Areas under ROC curves were calculated.

Results: There was a significant correlation between 24-hour protein excretion and the urine P/C ratio ($r = 0.828$, $p < 0.0001$). The cut-off P/C ratio for 300 mg per 24 h was 0.28: sensitivity and specificity were 60.4% and 77.9%, respectively. The positive predictive value (PPV) was 77.5% and negative predictive value (NPV) was 60.9%. The cut-off P/C ratio for 2000 mg per 24 h was 0.77: sensitivity and specificity were 96.8% and 98.6%, respectively. The PPV was 96.8% and NPV was 98.6%. Area under ROC curves for 24-hour urine total protein of 300-2000 mg/day and >2000 mg/day were 0.74 (95% CI 0.66-0.80) and 0.99 (95% CI 0.95-0.99), respectively.

Conclusions: Spot P/C ratio is a poor predictor of 24-hour proteinuria but can predict proteinuria >2000 mg better than 300-2000 mg.

1. Introduction

Preeclampsia is determined by the presence of elevated blood pressure and significant proteinuria ($\geq$300 mg per 24 h) after the 20th week of gestation [1]. Internationally, preeclampsia is a significant contributor to maternal and fetal mortality and it affects 2-8% of all pregnancies [2,3].

Proteinuria is an important sign of preeclampsia and the diagnosis is questionable in its absence. A level of 300 mg or more urine protein per 24-hour period is described as significant proteinuria, and urine collection over 24 hours is considered the traditional comparator for quantification of proteinuria in pregnancy. Waiting for 24-hour urine collection and results, however, can delay the diagnosis of preeclampsia. Also, it may not be possible to complete the urine collection when delivery occurs, leading to undetermined proteinuria status and an unsubstantiated diagnosis of preeclampsia [4–6]. Thus alternative methods including urinary dipsticks, urine collection over a shorter period, the spot urine protein-to-creatinine (P/C) ratio and spot albumin:creatinine ratio have been used to shorten the time period to diagnose preeclampsia [7,8]. Since 1980 some investigators have suggested the urinary spot P/C ratio for the diagnosis of preeclampsia and other hypertensive conditions [9]. While some studies have demonstrated a good correlation between urinary P/C ratio and 24-hour protein value [10–12], others did not show this correlation [13–15]. Because of these conflincting results, spot P/C ratio has not been widely used in obstetric practice.

In this study, we aimed to compare the spot urine P/C ratio and 24-hour urine protein excretion in pregnant women with preeclampsia, and also to determine the best discriminator values of the spot P/C ratios for 300 mg and 2000 mg per 24 h.

* Corresponding author. Tel.: +90 05053842092.
  E-mail address: emreerd@yahoo.com (E. Erdogdu).

2. Materials and methods

This prospective study included 200 pregnant women with suspicion of preeclampsia who did not have known intrinsic renal disease with proteinuria, chronic hypertension before pregnancy, bacteriuria or diabetes. All patients had new onset hypertension at or greater than 140/90 mmHg after 20 weeks of gestation. The study was conducted at Zeynep Kamil Research Hospital, a tertiary center, between September 2010 and June 2011. The local ethics committee approved the study design and a total of 200 participants provided written informed consent. Twenty-four hour urine was collected from outpatients or inpatients who had suspicion of preeclampsia as clinically indicated. Written instructions were given to patients for proper collection of a 24-hour urine specimen, and 24-hour urine creatinine excretion was used to assess the adequacy of 24-hour urine collection according to the general nephrology references [16]. A 24-hour urine creatinine excretion value below 15 mg/kg and above 20 mg/kg, calculated using pre-pregnancy weight, was considered as inadequate 24-hour urine collection. Repeat collections were not performed in cases who had inadequate collection. Cases who had incomplete 24-hour urine collection and proteinuria <300 mg were excluded.

Preeclampsia is considered as new-onset persistent hypertension after the 20th week of gestation with at or greater than 140/90 mmHg or urine protein >300 mg per 24 h. Twenty-four hour urine collection started from 8 am in the morning following admission. Spot urine P/C samples were gathered immediately after the 24-hour urine collection. A Foley catheter was not used for obtaining mid-stream urine sample. Urinary protein quantitation was done by the Biuret method, and urinary creatinine estimation was done by Jaffe's method [17,18]. Detailed medical and obstetric history including age, body mass index (BMI), gravida, parity, history of preeclampsia, family history of preeclampsia, and diabetes were recorded.

The correlation between 24-hour urine protein excretion and spot urine P/C ratio was analyzed with the Pearson correlation coefficient. Using protein values of 300 mg and 2000 mg on 24-hour collections, receiver operating characteristic (ROC) curves were constructed and the best P/C ratio cut-off was identified. Area under the ROC curve was calculated. Sensitivity, specificity and predictive values of the urine P/C at various cut-offs for prediction of significant proteinuria were estimated.

3. Results

A total of 200 pregnant women with suspicion of preeclampsia were selected; 186 (93%) and 14 (7%) of them completed the 24-hour urine collection as inpatients and outpatients, respectively. Characteristics of the 200 cases as inpatients and outpatients are shown in Table 1. Seventy-three cases were excluded, due to inadequate 24-hour urine collection in 36 (18%) patients and proteinuria below 300 mg/day in 37 (18.5%) patients.

A total of 127 patients (63.5%) who had 24-hour urine protein value of >300 mg were considered as preeclampsia: 94 patients had a 24-hour protein value of 300-2000 mg and 33 had >2000 mg. The demographic characteristics of the patients with

Table 1
Characteristics of 200 women with suspicion of preeclampsia as inpatients and outpatients {n (%), mean ± SD, or median [IQR]}.

	Inpatients (n = 186)	Outpatients (n = 14)
Age, years (median)	29.2 ± 4.8	28.3 ± 4.7
Gravidity (n)	2.4 ± 1.5	3.2 ± 1.4
Parity (n)	0.9 ± 1.1	1.1 ± 1.1
Prepregnancy weight (kg)	74.3 ± 16.2	72.2 ± 14.5
24 hour urine protein (g)	0.8 [0.2–2.8]	0.4 [0.1–0.6]
Proteinuria 300-2000 mg/24 h (%)	54.8	28.5
Proteinuria >2000 mg/24 h (%)	12.2	0
Inadequate collection (%)	17	28.5

Table 2
Demographic characteristics of 127 participants with preeclampsia.

	Mean + SD or n	IQR or %
Age, years (median)	29.1 ± 5.8	21-38
Gravidity (n)	2.2 ± 1.5	1-6
Parity (n)	0.9 ± 1.4	0-5
Abortion (n)	0.3 ± 0.8	0-4
Body mass index (kg/m^2)	30.9 ± 5.8	22-37.5
Previous history of preeclampsia (n)	32	24.6%
Family history of hypertension (n)	30	24%
Family history of diabetes mellitus (n)	61	47.6%

IQR, interquartile range.

preeclampsia are shown in Table 2. The mean age was 29.1 ± 5.8 years and the mean gestational age was 33.5 ± 5.2 weeks. The mean urinary protein excretion of 24-hour urine collections in group with 300-2000 mg and >2000 mg were 669 ± 432 mg and 2900 ± 642 mg, respectively. By the ROC curve analysis, a P/C ratio of 0.28 was identified as the best threshold to detect urine protein excretion of 300 mg per 24 h, with a sensitivity and a specificity of 60.4% and 77.9%, respectively. The positive predictive value (PPV) and negative predictive value (NPV) were 77.5% and 60.9%, respectively. A spot P/C ratio less than 0.19 could exclude preeclampsia with a sensitivity of 100%. The best threshold of the P/C ratio to detect urine protein excretion >2000 mg per 24 h was 0.77, with a sensitivity and a specificity of 96.8% and 98.6%, respectively. With this cut-off, PPV was 98.8% and NPV was 98.6% (Table 3). The areas under the ROC curves for 300 and 2000 mg of protein per 24-hour were 0.74 and 0.99, respectively (Figs. 1 and 2).

4. Comments

Assessment of urinary protein is mandatory to establish the diagnosis of preeclampsia. Measurement of protein excretion in a 24-hour urinary collection is the gold standard for the quantitative evaluation of proteinuria in pregnancy, when significant proteinuria is defined as proteinuria of 300 mg/day or more [4]. The urine requires refrigeration, however, and its collection is cumbersome and time-consuming for women and clinicians. Also, the results may be misleading if collected inaccurately. Outside pregnancy the 24-hour urine collection has well-documented problems with completeness, timeliness, and ease of performance. In pregnancy, problems are increased by the physiological dilation of the ureters

Table 3
Test performance of spot P/C ratio assessment for 24-hour urine protein results.

24-hour urine protein (mg)	Optimal spot P/C (mg/mg)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Positive likehood ratio	Negative likehood ratio
300	0.28	60.4	77.8	77.5	60.9	2.72	0.51
2000	0.77	96.8	98.6	96.8	98.6	6.97	0.03