A Comparison of Spot Urine Protein-Creatinine Ratio With 24-hour Urine Protein Excretion in Women With Preeclampsia

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Introduction. Proteinuria is an important diagnostic component of preeclampsia. We prospectively compared the results of spot urine protein-creatinine (P/C) ratio with 24-hour urine protein excretion in women with preeclampsia.

Materials and Methods. A total of 81 pregnant women with preeclampsia were prospectively studied for proteinuria. Urine P/C ratio was determined in a spot mid-stream urine sample, and the amount of protein excretion was measured in 24-hour urine collected on the subsequent day. The correlation between the spot P/C ratio and 24-hour urine protein excretion was assessed. Diagnostic value of P/C ratio was expressed in terms of specificity and sensitivity. The receiver operating characteristic curve analysis was used to determine the best discriminator values of the spot urine P/C ratios for preeclampsia (proteinuria ≥ 300 mg/24 h).

Results. There was a strong correlation between the spot P/C ratio and 24-hour urine protein excretion (r = 0.84; $P < .001$). The optimal spot P/C ratio cutoff point was 0.20 for 300 mg/24 h of protein excretion (preeclampsia), with a sensitivity, specificity, positive predictive value, and negative predictive value of 91.2%, 87.8%, 94.4%, and 96.8%, respectively. The spot P/C ratios less than 0.19 yielded a sensitivity of 100% for exclusion of preeclampsia.

Conclusions. We found that there is a significant correlation between the spot urine P/C ratio and 24-hour urine protein excretion in women with preeclampsia. Urine P/C ratio could be used for exclusion of preeclampsia.

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INTRODUCTION

Preeclampsia, a common cause of maternal morbidity, occurs in up to 2% to 8% of all pregnancies.[1] As a result, obstetricians should be on the alert for any sign of this hazardous complication among women in the third trimester. In case of increased blood pressure, detailed laboratory evaluations, including assessment of urine, blood, and liver function are essential. Measurement of protein excretion in a 24-hour urine collection has been the long-standing gold-standard but time consuming test for the quantitative evaluation of proteinuria induced by preeclampsia. A more rapid test capable of accurately predicting the results of a 24-hour urine would be valuable. An alternative method for quantitative evaluation of proteinuria is the measurement of protein-creatinine (P/C) ratio in a spot urine sample, which avoids the influence of variations in urinary solute concentration and provides a more convenient and rapid method to assess protein excretion.

Clinical utility of urine P/C ratio as a substitute of

24-urine protein excretion for detecting significant proteinuria in patients with preeclampsia still remains unclear. Some investigators have proposed the use of a spot urine P/C ratio.[2,3] However, there are some reports with conflicting results,[4,5] and the variability in cutoff values between studies does not allow a uniform recommendation. We examined the correlation between spot urine P/C ratio and 24-hour urine protein excretion in patients being evaluated for preeclampsia.

MATERIALS AND METHODS

Patients

Pregnant women who were admitted in our obstetrics department with a suspicion of preeclampsia were studied prospectively. The study was conducted at Imam Khomeini Hospital in Ahwaz, Iran, a tertiary care center, between March 2006 and September 2007, and the local ethics committee approved the study design. Preeclampsia was defined as a blood pressure of 140/90 mm Hg or higher after the 20th week of gestation and a urine protein of 1+ or greater by dipstick test or chronic hypertension without proteinuria before the 20th week accompanied by new-onset urine protein of 1+ or greater by dipstick test. Women with the following conditions were excluded: a known kidney disease, heavy exercise (more than 1 hour of vigorous exercise on the day of urine collection), bacteriuria, bed rest longer than 24 hours, and gestational diabetes mellitus. In addition, women who delivered their babies during the urine collection day were excluded. A total of 81 pregnant women meeting the inpatient admission criteria for the evaluation of preeclampsia were prospectively recruited and provided informed written consent.

Urine Tests

Urine was collected for 24 hours. Immediately prior to the collection period, the patients also provided a spot mid-stream urine sample. The urine P/C ratio was determined on spot urine specimens. The concentration of total protein in urine was measured by a biuret colorimetric assay (Cobas Integra Analyzer, F Hoffman-La Roche, Basel, Switzerland), and the urine creatinine level was measured by a modified Jaffe test (Hitachi 7170 autoanalyzer, Hitachi, Tokyo, Japan). The urine P/C ratio was obtained by dividing the urinary protein concentration by the urine creatinine concentration. Measurements on the 24-hour urine sample were performed on the same day as collections were completed.

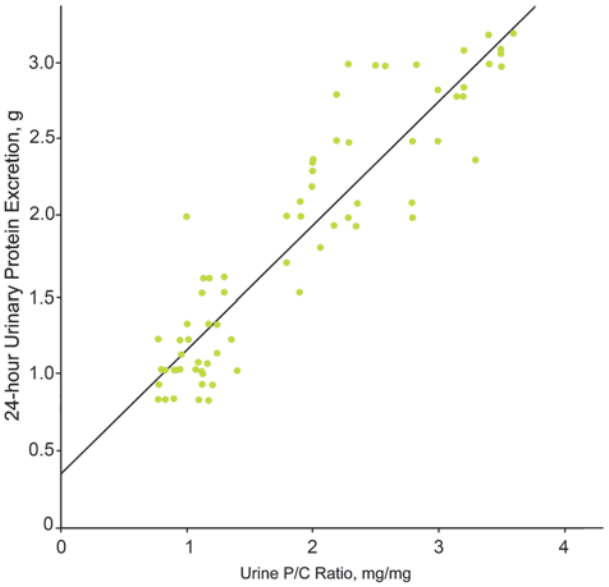
Statistical Analyses

The correlation between P/C ratio in spot urine samples and urinary protein excretion in 24-hour collections were analyzed. Sensitivity, specificity, and predictive values of the random urine P/C ratio at various cutoffs for prediction of significant proteinuria were estimated considering the 24-hour urinary protein excretion as the gold standard. The receiver operating characteristic (ROC) curve was used, and the area under the curve (AUC) was calculated. The relationship between the urine P/C ratio and the 24-hour protein excretion was assessed with the Pearson correlation test. Descriptive statistics were used for demographic and baseline data and summarized as mean ± standard deviation, median, and percentage, where appropriate. A P value less than .05 was considered significant. The SPSS software (Statistical Package for the Social Sciences, version 11.0, SPSS Inc, Chicago, Ill, USA) and the MedCalc software (version 9.3.0.0, MedCalc, Mariakerke, Belgium) were used for the analyses.

RESULTS

A total of 117 pregnant women with preeclampsia were selected, of whom 36 were excluded because of gestational diabetes mellitus in 12, bacteriuria in 10, delivery before the completion of their 24-hour urine collection in 8, inadequate 24-hour urine collection in 3, and refusing to continue the study in 3. Finally, 81 eligible pregnant women completed the study. Their mean age was 26.5 ± 3.6 years (range, 17 to 36 years). Four patients had preexisting hypertension with superimposed preeclampsia. Their mean gestational age was 34.4 ± 4.7 weeks (range, 21 to 41 weeks).

The median serum creatinine concentration was 0.52 mg/dL, and the mean urinary protein excretion in 24-hour urine collections was 1.79 ± 0.80 g/dL (range, 120 mg/dL to 3200 mg/dL). The mean P/C ratio was 1.84 ± 0.91 (range, 0.38 to 3.60). The correlation coefficient for the P/C ratio against the 24-hour urine protein excretion was 0.84. The regression equation was Y = 0.81 X + 0.3 (P < .001; Figure) where Y indicates urinary



There was a strong correlation between the spot protein-creatinine ratio and 24-hour urine protein excretion value (r = 0.84; *P* < .001).

protein excretion (g/24 h) and X indicates P/C ratio. By the ROC curve analysis, the P/C ratio of 0.20 was identified as the best threshold to detect urine protein excretion of 300 mg/24 h, with a sensitivity and a specificity of 91.2% and 87.8%, respectively. The positive and negative predictive values for P/C ratios 0.20 were 94.4% and 96.8%, respectively. A spot P/C ratio les than 0.19 could exclude preeclampsia with a sensitivity of 100%.

DISCUSSION

Preeclampsia is a significant contributor to maternal mortality and it affects 2% to 8% of all pregnancies.[1] Obstetricians always look for evidence of preeclampsia in the third trimester. Concerns typically arise when patients present with increased blood pressure. One of the ways to diagnose preeclampsia, apart from the blood pressure criteria, is to look for the presence of significant proteinuria. The gold standard for proteinuria, a key component in the assessment of preeclampsia, is a 24-hour urine collection, which is cumbersome both for the patients and the staff handling the urine collection, and subject to error due to inaccurate timing and/or incompleteness.[6] Previous studies have demonstrated inadequate collected urine volumes in up to 37% of samples. Waiting for the results of 24-hour urine collection can often delay diagnosis of preeclampsia. Accurately substitution of a spot urine P/C ratio for a 24-hour urine collection would have significant implications including facilitation of prompt clinical decision making. This would also impact healthcare costs and improve patients' satisfaction with care, too. The objective of our study was to compare these two methods of assessing urinary protein: spot urine P/C ratio as a useful rapid test and 24-hour urine protein excretion as the gold-standard test. We prospectively determined the correlation between spot urine P/C ratio and 24-hour urine protein excretion. Urine was collected from patients who met admission criteria for preeclampsia, and the spot value obtained at the beginning of the 24-hour collection period was compared to the result acquired from the 24-hour collection to see if these values were correlated.

A good correlation between the spot urine P/C ratio and 24-hour protein excretion has been demonstrated in patients with diabetic nephropathy, lupus nephritis, chronic kidney disease, and transplanted kidneys.[7-10] The National Kidney Foundation guidelines have suggested that spot urine samples should be used to detect and monitor proteinuria in children and adults.[11] In our study, a urine P/C ratio of 0.20 corresponded with a protein excretion rate of 300 mg/24 h. These are characterized by excellent accuracy. Consistent with most previous studies with correlation coefficients ranging between 0.80 and 0.97, we found a strong correlation (r = 0.84) between the spot P/C ratio and the 24-hour urine protein.[12-15] However, using the spot P/C ratio of 0.20 as a correlate to the critical value of 300 mg of protein over 24 hours would result in the failure to identify significant proteinuria in approximately 8.8% of affected patients.

There are some reports with conflicting results. Because of the variability in laboratory methods for measuring proteinuria in different reported studies, several cutoff points and different units for the urinary P/C ratio have been reported, thereby precluding valid comparisons among such studies.[16-18] In a study by Durnwald and Mercer, the authors determined lower correlation coefficients of 0.56 and 0.41 and cautioned against substituting spot P/C ratio for the 24-hour urine protein collection.[4] They showed a poor correlation between the random urinary P/C ratio and the 24-hour urine total protein. In addition, the ROC

analysis found no clear shoulder even though the AUC was 0.80. Their optimal cutoff value for P/C ratio was 50.4 which had a 72.6% sensitivity and a 73.1% specificity.[4] The difference of findings between their report and ours may be due to the difference in the study population. The wider exclusion criteria in our population may explain the higher positive and negative predictive values found in our study, as diabetes mellitus and preexistence hypertension may lead to elevation in urine albumin. Furthermore, Durnwald and Mercer[4] also recruited outpatient participants, who could have incomplete urine collections, which may be associated with lower levels of 24-hour urine total protein that increases the false negative rate.

Wheeler and colleagues assessed the use of spot urine P/C ratio for detecting significant proteinuria in 126 women with preeclampsia.[18] In their study, a urine P/C ratio of 0.21 corresponded with a protein excretion rate of 300 mg/24 h. The AUC was 0.86, indicating good accuracy. Moreover, P/C ratios of 0.46, 0.82, and 3.0 represented 1000 mg/24 h, 2000 mg/24 h, and 5000 mg/24 h, respectively, and the matching AUCs were 0.91, 0.98, and 1.0, respectively. All of these were characterized by excellent accuracy. The study demonstrated that although there is a strong correlation between spot urine P/C ratio and the 24-hour urine protein excretion, they cannot be viewed equal in their ability to measure proteinuria quantitatively. The 24-hour urine collection should remain the gold standard for evaluation for preeclampsia.

Our data suggested that the random urine P/C ratio is a highly accurate test for discriminating between insignificant and significant proteinuria, as demonstrated by an area under the ROC curve of 0.92. The main concern in clinical use of this test is the false-negative test results, because 8% of patients with preeclampsia may be missed. To obtain the optimal cutoff, we selected the one that while increasing specificity maintains a sensitivity of higher than 90% in order to reduce the possibility of missing the diagnosis of preeclampsia. Research in the future should be focused on the evaluation of clinical outcomes and the cost-effectiveness of the use of a random urinary P/C ratio for prediction of significant proteinuria. In addition, studying the test in an outpatient basis should be further considered in order to apply it in ambulatory management of preeclamptic patient. We suggest that the test be done also in severely preeclamptic women, as they tend to excrete greater amounts of protein, in order to determine a cutoff value for prediction of the 24-hour urine protein excretion of greater than 5 g.

CONCLUSIONS

Based on the findings of the present study, we conclude that a random urine P/C ratio predicts the amount of 24-hour urine protein excretion with a highly accuracy. This test could be a reasonable alternative to the 24-hour urine collection for detection of significant proteinuria in hospitalized pregnant women with suspected preeclampsia. From our ROC curve analyses, we believe that the P/C ration in urine should be considered as a potential substitute for 24-hour urine collection in pregnant women.

CONFLICT OF INTEREST

None declared.

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