Comparison of 12-hour Urine Protein and Protein: Creatinine Ratio with 24-hour Urine Protein for the Diagnosis of Preeclampsia

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Published In/Presented At

Tun, C., Quiñones, J., Kurt, A., Smulian, J., & Rochon, M. (2012). Comparison of 12-hour urine protein and protein:creatinine ratio with 24-hour urine protein for the diagnosis of preeclampsia. American Journal Of Obstetrics And Gynecology, 207(3), 233.e1-8.

Comparison of 12-hour urine protein and protein:creatinine ratio with 24-hour urine protein for the diagnosis of preeclampsia

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OBJECTIVE: The purpose of this study was to evaluate the performance of the 12-hour urine protein >165 mg and protein:creatinine ratio >0.15 for the prediction of 24-hour urine protein of ≥300 mg in patients with suspected preeclampsia.

STUDY DESIGN: We performed a prospective observational study of 90 women who had been admitted with suspected preeclampsia. Protein:creatinine ratio and 12- and 24-hour urine specimens were collected for each patient. Test characteristics for the identification of 24-hour urine protein ≥300 mg were calculated.

RESULTS: A 12-hour urine protein >165 mg and protein:creatinine ratio of >0.15 correlated significantly with 24-hour urine protein ≥300 mg ($r = 0.99$; $P < .001$; and $r = 0.54$; $P < .001$, respectively). A 12-hour urine protein >165 mg performed better than protein:creatinine ratio as a predictor of a 24-hour urine protein ≥300 mg (sensitivity, 96% and 89%; specificity, 100% and 49%; positive predictive value, 100% and 32%; negative predictive value, 98% and 91%, respectively).

CONCLUSION: The high correlation of a 12-hour urine protein >165 mg with a 24-hour urine protein ≥300 mg (with the benefit of a shorter evaluation time) and the high negative predictive value of protein:creatinine ratio suggest that the use of both these tests have a role in the evaluation and treatment of women with suspected preeclampsia.

Key words: 12-hour urine protein, 24-hour urine protein, preeclampsia, protein:creatinine ratio

Cite this article as: Tun C, Quiñones JN, Kurt A, et al. Comparison of 12-hour urine protein and protein:creatinine ratio with 24-hour urine protein for the diagnosis of preeclampsia. Am J Obstet Gynecol 2012;207:233.e1-8.

Hypertensive disease occurs in approximately 5-10% of pregnancies[1] and is responsible for approximately 15% of maternal deaths in the developed countries.[1-3] The exact incidence of preeclampsia in the United States is not known; however, it is estimated to range from 6–8% of all pregnancies and remains a leading cause of maternal and neonatal mortality and morbidity worldwide.[4] It is a pregnancy-specific syndrome of reduced organ perfusion that is related to vasospasm and activation of the coagulation cascade.[2]

Multiple causes have been hypothesized for preeclampsia, including abnormal trophoblast invasion of uterine blood vessels, immunologic intolerance between fetoplacental and maternal tissues, maladaptation to the cardiovascular changes or inflammatory changes of pregnancy, dietary deficiencies, and genetic abnormalities.[4] Risk factors that are associated with preeclampsia include nulliparity, multifetal gestation, obesity, maternal age >35 years, African American ethnicity, family history of preeclampsia-eclampsia, preeclampsia in previous pregnancy, abnormal Doppler studies at 18 and 24 weeks, pregestational diabetes mellitus, presence of thrombophilias, hypertension, and renal disease.[1,3,4]

Preeclampsia is associated with increased risk of maternal and fetal morbidity and mortality. These depend on the gestational age at onset of preeclampsia, timing of delivery, the severity of disease process, presence of multifetal gestation, and the presence of preexisting medical conditions such as pregestational diabetes mellitus, renal disease, or thrombophilias. In women with mild preeclampsia, the perinatal death rate and rates of preterm delivery, small-for-gestational-age infants, and abruptio placentae are similar to those of normotensive pregnancies.[4]

The standard threshold value for proteinuria in the setting of hypertension for the diagnosis of preeclampsia is a 24-hour urine protein ≥300 mg. Urine dipstick, protein:creatinine ratio, and 12-hour urine protein collection have been compared with the 24-hour urine protein as methods of quantitating proteinuria in pregnancy in the hope of finding a test that is more readily available, easy to perform, inexpensive, and that yields a quick result. However, evaluation of a timed collection as opposed to a random specimen has been classically recommended because protein excretion is variable in the setting of preeclampsia.[1-4] Preliminary studies have suggested that 12-hour urine protein collection (as opposed to a 24-hour urine pro-

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Received March 13, 2012; revised May 5, 2012; accepted June 5, 2012.

Supported by the Lehigh Valley Health Network Department of Obstetrics and Gynecology Research Fund.

The authors report no conflict of interest.

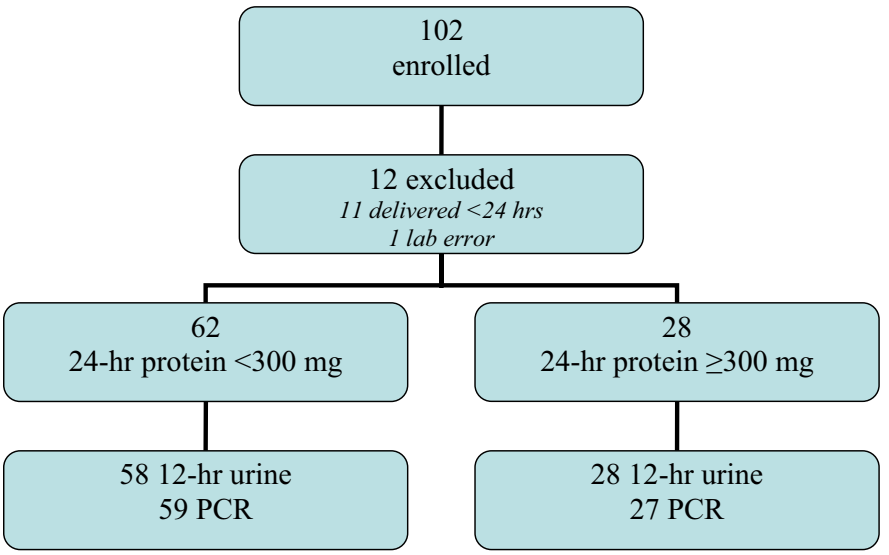
Presented at the 32nd annual meeting of the Society for Maternal-Fetal Medicine, Dallas, TX, Feb. 6-11, 2012.

Reprints not available from the authors.

0002-9378/$36.00

http://dx.doi.org/10.1016/j.ajog.2012.06.010

FIGURE 1
Enrollment flowchart



Lab, laboratory; *PCR*, protein:creatinine ratio.

Tun. Twelve-hour urine protein and PCR vs 24-hour urine protein. Am J Obstet Gynecol 2012.

tein collection) and/or protein:creatinine ratio may be adequate for the evaluation of preeclampsia with the advantage of an earlier diagnosis and treatment of preeclampsia as well as the potential for earlier hospital discharge and increased compliance with specimen collection.[5-8]

Adelberg et al,[6] in a prospective observational study of 65 patients, used receiver operating characteristic (ROC) curves to determine the optimal cutoff for proteinuria (>165 mg protein) in the 12-hour sample to diagnose preeclampsia accurately (with 78% sensitivity, 100% specificity, 100% positive predictive value, and 71% negative predictive value; $P < .001$). Similarly, Schubert and Abernathy,[7] in a small observational study of 15 patients, identified an optimal protein:creatinine cutoff of >0.15 (with 100% sensitivity, 50% specificity, 75% positive predictive value, 100% negative predictive value) for the diagnosis of preeclampsia. However, these cutoffs have not been tested prospectively. The purpose of our study was to determine prospectively the performance of the 12-hour urine protein >165 mg and protein:creatinine ratio >0.15 for the prediction of 24-hour urine protein ≥300 mg in patients undergoing evaluation for preeclampsia.

Materials and Methods

This was a prospective observational study of pregnant women aged 18-55 years and >20 weeks' gestation who were admitted to the Lehigh Valley Health Network antepartum unit who were undergoing a 24-hour urine collection for the diagnosis and/or management of preeclampsia from July 1, 2010 to December 31, 2011. Women were excluded if they had known prepregnancy renal disease (defined as baseline 24-hour urine protein ≥300 mg), had a clinical indication for delivery at the time of admission, were outside the maternal or gestational age parameters as defined earlier, did not speak English, did not give informed consent for any reason, or had been enrolled previously in the study.

Spot urine for protein:creatinine ratio, 12-hour urine collection, and 24-hour urine collection were obtained for each patient. The 24-hour urine collection was started at the time of admission, regardless of the time of day, in a standard fashion. For study purposes, the 24-hour urine specimen was collected in 2 consecutive 12-hour urine collections. Each container was marked with the patient's name, medical record number, number of the container, and collection time. The protein:creatinine ratio was sent on the initial urine specimen (which was otherwise discarded, consistent with standard timed urine collection protocol). We chose to send the protein:creatinine ratio on this specimen, as opposed to the timed collection, to simulate how the protein:creatinine ratio would be used in clinical practice (at the time of presentation). In a small number of subjects, the protein:creatinine ratio was erroneously not collected on the initial urine specimen and was therefore collected either from the timed specimen itself or immediately after the timed collection was completed. The containers were sent to the Lehigh Valley Hospital Health Network Laboratories for analysis. The urine volume, total protein, and creatinine level were measured to determine the protein:creatinine ratio, 12-hour urine protein, and 24-hour urine protein. Only the 24-hour urine result was used for clinical management; providers were blinded to the results of the protein:creatinine ratio and 12-hour urine protein. Antepartum management was otherwise routine and at the discretion of the patient's provider and institutional clinical protocol, which included modified bed rest, laboratory evaluation for HELLP (hemolysis elevated liver enzymes low platelets) syndrome, and serial assessment of maternal blood pressure.

Analysis for protein in the first 12-hour urine sample was performed by Lehigh Valley Hospital Health Network Laboratories with the use of an urine assay (ADVIA Total Protein [urine] assay; Siemens Healthcare Diagnostics Inc., Tarrytown, NY), which is a modified Fujita method. This was the routine commercial assay that was used by the Health Network Laboratories for calculating total urine protein. The assay consisted of aspirating 30 μL of the urine sample and making 1:5 dilution with 120 μL of on-system isotonic saline solution to make a "working dilution," then 13.3 μL of the "working dilution" was dispensed into a cuvette that contained 80 μL of UPRO_2 R1 reagent (ADVIA Total Protein [urine] assay) and was incubated in the oil bath at 37°C for 10 minutes. The resulting blue-colored complex was read at 596/694 nm to determine the protein con-

TABLE 1
Baseline maternal characteristics by 24-hour urine protein result

Variable	24-hr protein <300 mg (n = 62)	24-hr protein ≥300 mg (n = 28)	*P* value
Maternal age, y[a]	29 (19-42)	30 (19-38)	.76
Race/ethnicity, n (%)			.41
White	49 (79)	22 (79)	
Black	2 (3)	3 (11)	
Asian	3 (5)	0	
Hispanic	1 (2)	1 (4)	
Private insurance, n (%)	45 (73)	20 (71)	.91
Multiparous, n (%)	29 (47)	20 (71)	.03
Multiple gestation, n (%)	8 (13)	3 (11)	.77
Body mass index, kg/m^2[a]	33.1 (19.5–69.9)	36.4 (25.4–54.9)	.13
Gestational age, wk[a]	34.3 (25.9–39.0)	32.8 (24.0–35.4)	.007
Smoking, n (%)	13 (21)	4 (14)	.45
Any comorbidity, n (%)[b]	57 (91)	26 (93)	.88
Chronic hypertension	12 (19)	8 (29)	.33
Gestational hypertension or preeclampsia	15 (24)	7 (25)	.93
Pregestational diabetes mellitus	1 (2)	4 (14)	.015
Gestational diabetes mellitus	8 (13)	6 (21)	.30
Indication for admission, n (%)[b]			
Elevated blood pressure	51 (82)	26 (93)	.19
Proteinuria	16 (26)	19 (68)	< .001
Symptoms[c]	28 (45)	14 (50)	.67
Laboratory abnormalities	7 (11)	11 (39)	.002
Fetal growth restriction	10 (16)	3 (14)	.50
Other[d]	9 (15)	6 (21)	.42
Previous 24-hr urine protein done, n (%)	31 (50)	19 (68)	.11
Previous 24-hr urine protein, mg[a]	155 (50–440)	210 (64–2240)	.14
Median systolic blood pressure on admission, mm Hg[a]	137 (105–168)	140 (117–158)	.51
Median diastolic blood pressure on admission, mm Hg[a]	83 (55–103)	82 (64–112)	.85
Median systolic blood pressure during collection, mm Hg[a]	131 (99–165)	136 (105–152)	.11
Median diastolic blood pressure during collection, mm Hg[a]	76 (53–98)	78 (55–99)	.41

[a] Data are in median (range); [b] Subject may have >1; [c] Includes headache, scotomata, abdominal pain, and significant weight gain that was associated with edema; [d] Includes shortness of breath, seizure of uncertain origin, oligohydramnios, visual changes other than scotomata.

Tun. Twelve-hour urine protein and PCR vs 24-hour urine protein. Am J Obstet Gynecol 2012.

centration in milligrams per deciliter. Total protein for the 12-hour urine was calculated by multiplying the total urine volume (dL) by the concentration of protein in the test sample (mg/dL) and was considered diagnostic for preeclampsia if the result was >165 mg. Total protein for the 24-hour urine protein was calculated by combining both 12-hour urine specimens and running the Health Network Laboratories ADVIA Total Protein assay as described previously. It was considered diagnostic for preeclampsia if the result was ≥300 mg. Creatinine clearance was calculated on the 24-hour urine sample by standard methods as a routine part of the preeclampsia workup. Spot urine for protein:creatinine ratio was calculated by random urine protein (mg/dL)/random urine creatinine (mg/dL) and was considered diagnostic for preeclampsia if the result was >0.15.

The primary outcome was test characteristics of protein:creatinine ratio >0.15 and 12-hour urine protein >165 mg to predict a 24-hour urine protein ≥300

TABLE 2
Pregnancy outcome by 24-hour urine protein result[a]

Variable	24-hr protein <300 mg (n = 58)	24-hr protein ≥300 mg (n = 27)	*P* value
Delivery during study admission, n (%)[b]	19 (33)	18 (67)	.003
Gestational age at delivery, wk[c]	37.0 (27.3–40.6)	34.3 (24.9–38.1)	< .001
Induction, n (%)	30 (52)	16 (59)	.47
Indication for induction, n (%)[d]			
Hypertension/preeclampsia	22 (38)	13 (48)	.55
Growth restriction	4 (7)	0 (0)	.13
Oligohydramnios	3 (5)	1 (4)	.68
Fetal death	0	2 (7)	.048
Preterm premature rupture of membranes	1 (2)	1 (4)	.64
Maternal medical condition	1 (2)	0	.46
Other	2 (3)	0	.29
Cesarean delivery, n (%)	33 (57)	17 (63)	.66
Maternal preeclampsia morbidity, n (%)[d]	18 (31)	12 (44)	.23
Eclampsia	1 (2)	0	.49
Pulmonary edema	0	1 (4)	.14
HELLP syndrome (hemolysis elevated liver enzymes low platelets)	1 (2)	1 (4)	.58
Abruption	2 (3)	0	.33
Fetal death	0	2 (7)	.04
Growth restriction	13 (22)	8 (30)	.49
Transfusion	3 (5)	1 (4)	.77
Other[e]	2 (40)	3 (11)	.20
Birthweight, g[c]	2733 (600–4025)	2100 (425–3815)	.004
Male sex, n (%)	29 (50)	13 (48)	.83
5-minute Apgar score <7, n (%)	0	1 (4)	.28
Arterial cord pH[c]	7.27 (7.06–7.38)	7.27 (7.01–7.36)	.78
Neonatal intensive care unit admission, n (%)	30 (52)	18 (67)	.17
Intrapartum/Neonatal demise, n (%)	0 (0)	3 (11)	.006

PPROM, preterm premature rupture of membranes.

[a] Available for 85 patients; [b] Admission during which study collection took place; [c] Data are in median (range); [d] Subjects may have >1; [e] Includes wound hematoma, readmission for severe preeclampsia, pleural effusion, postpartum thrombocytopenia, and postpartum hemorrhage.

Tun. Twelve-hour urine protein and PCR vs 24-hour urine protein. Am J Obstet Gynecol 2012.

mg. Baseline maternal characteristics (which included age, ethnicity, parity, insurance type, gestational age at admission, indication for admission, comorbidities, and blood pressure during admission) and delivery outcomes (which included gestational age at delivery, induction indication, mode of delivery, preeclampsia complications, and neonatal outcomes) were collected, and the data for patients with and without a 24-hour urine protein ≥300 mg were compared. For a few subjects, pregnancy outcomes were not available because they delivered at an outside hospital. The sensitivity, specificity, and positive and negative predictive values were calculated for the 12-hour urine protein >165 mg and protein:creatinine ratio >0.15; a 24-hour urine protein ≥300 mg served as the reference. Correlation coefficient and ROC curves were generated for the 12-hour urine protein and protein:creatinine ratio vs the 24-hour urine protein.

Our hypothesis was that at least the 12-hour urine protein would perform very well as a predictor of 24-hour urine protein ≥300 mg. We based our initial sample size estimate on the ability of the 12-hour protein level of >165 mg to detect the abnormal 24-hour level. We assumed that approximately 40% of subjects would have the abnormal 24-hour protein level of ≥300 mg. We used an alpha level of .05 and beta level of .2 for our calculation. Based on this assess-

ment, we estimated that, to be able to have a sensitivity of 90% for the 12-hour sample to identify the abnormal 24-hour sample, we would need a total of 150 subjects to be enrolled (75 per group) with up to a 10% attrition rate. An interim analysis was performed after approximately two-thirds of the sample size was achieved to determine what additional resources would be needed. That analysis showed a higher sensitivity than expected, so enrollment was stopped early after 102 patients were enrolled. Data were analyzed with Stata statistical software (version 9.0; StataCorp, College Station, TX). The Student *t* test, χ^2 test, Mann Whitney *U* test, and Fisher's exact test were used to compare characteristics of women with and without 24-hour urine protein ≥300 mg. A probability value of < .05 was considered statistically significant. Institutional review board approval was obtained.

Results

One hundred two patients were enrolled in the study (Figure 1). Twelve subjects were subsequently excluded: 11 women did not complete the 24-hour urine protein collection because of a clinical indication for delivery and one woman's sample was processed incorrectly in the laboratory; the final cohort comprised 90 subjects. In addition, 4 spot urine samples for protein:creatinine ratio were inadvertently not collected, and four 24-hour urine collections were not separated into two 12-hour jugs for a total of 86 subjects with protein:creatinine ratio and 86 subjects with a 12-hour urine sample (Figure 1). Twenty-eight subjects (31%) had a 24-hour urine protein ≥300 mg. Baseline maternal characteristics by 24-hour urine category are summarized in Table 1. Women with a 24-hour urine protein ≥300 mg were more likely to be multiparous (71% vs 47%; $P = .03$) and have pregestational diabetes mellitus (14% vs 2%; $P = .015$). They were also admitted at an earlier median gestational age (32.8 weeks [range, 24.0–35.4 weeks] vs 34.3 weeks [range, 25.9–39.0 weeks]; $P = .007$) and were more likely to have proteinuria or abnormal laboratory values as part of their criteria for admission (68% vs 26% [$P < .001$] and 39% vs 11% [$P = .002$]). Baseline characteristics, including median systolic and diastolic blood pressures at time of admission and during collection period, were otherwise similar.

TABLE 3
Urine collection characteristics by 24 hour urine protein result

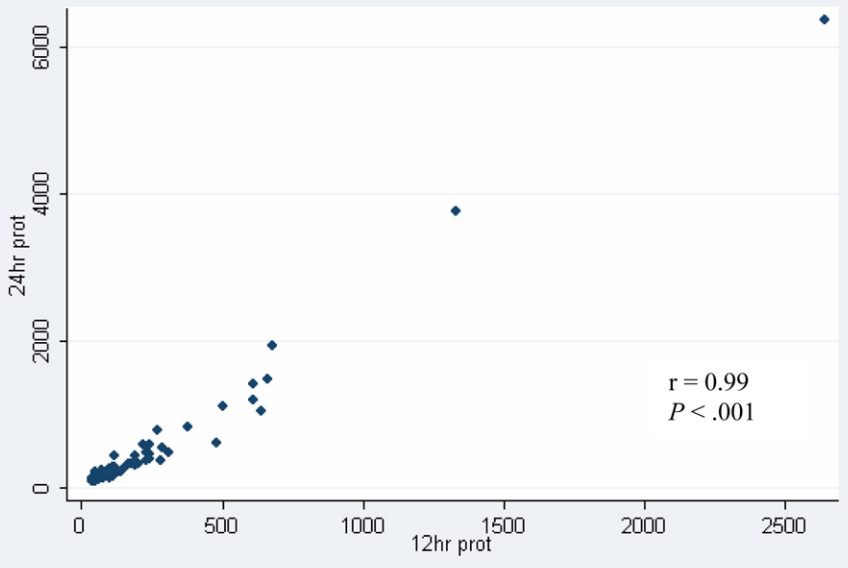
Variable	24-hr protein <300 mg (n = 62)	24-hr protein ≥300 mg (n = 28)	*P* value
24-hr			
Urine protein, mg[a]	175 (90–290)	520 (310–6360)	< .001
Urine volume, mL[a]	2300 (700–4700)	1825 (600–5100)	.23
Urine creatinine clearance, mL/min[a]	153 (59–272)	135 (80–283)	.51
12-hr			
Urine protein, mg[a]	70 (40–150)	255 (120–2640)	< .001
Urine volume, mL[a]	1050 (400–2300)	1050 (300–3050)	.97
Urine protein >165 mg, n (%)	0	27 (96)	< .001
Protein:creatinine ratio[a]	0.16 (0.07–0.5)	0.35 (0.14–4.57)	< .001
Protein:creatinine ratio >0.15, n (%)	30 (52)	24 (89)	.001

[a] Data are in median (range).

Tun. Twelve-hour urine protein and PCR vs 24-hour urine protein. Am J Obstet Gynecol 2012.

Pregnancy outcomes were available for 85 women and are summarized in Table 2 by 24-hour urine protein category. Women with a 24-hour urine protein ≥300 mg delivered at an earlier median gestational age (34.3 weeks [range, 24.9–38.1 weeks] vs 37.0 weeks [range, 27.3–40.6 weeks]; $P < .001$), had a lower median neonatal birthweight (2100 g [range, 425–3815 g] vs 2733 g [range, 600–4025 g]; $P = .004$), and were more likely to be delivered during the index admission (67% vs 33%; $P = .003$). They

FIGURE 2
Twelve-hour urine protein vs 24-hour urine protein



Prot, protein.

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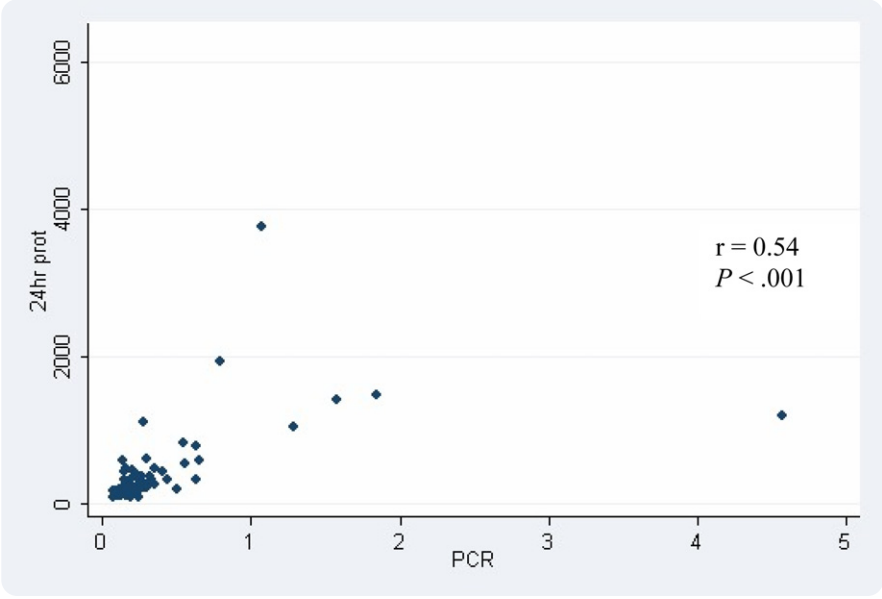
FIGURE 3
Protein:creatinine ratio vs 24-hour urine protein



PCR, protein:creatinine ratio; *prot*, protein.

Tun. Twelve-hour urine protein and PCR vs 24-hour urine protein. Am J Obstet Gynecol 2012.

were also more likely to experience an intrauterine fetal demise or intrapartum/neonatal demise. There was no difference in overall rates of preeclampsia morbidity, induction rates, cesarean delivery rates, or rates of neonatal intensive care unit admission.

Urine collection characteristics by 24-hour urine protein category are summarized in Table 3. As expected, median 24-hour, 12-hour urine protein and protein:creatinine ratio were higher in the 24-hour urine protein ≥300 mg group. There was no difference in urine volume or creatinine clearance between 24-hour urine groups. No subjects with a 24-hour urine protein <300 mg had a 12-hour urine protein >165 mg; in contrast, 52% of subjects with a 24-hour urine protein <300 mg had a protein:creatinine ratio of >0.15.

Both 12-hour urine protein and protein:creatinine ratio correlate significantly with 24-hour urine protein (r = 0.99; $P < .001$; and r = 0.54; $P < .001$, respectively; Figures 2 and 3). Performance of protein:creatinine ratio >0.15 and 12-hour urine protein >165 mg for the prediction of a 24-hour urine protein ≥300 mg are summarized in Table 4. A 12-hour urine protein >165 mg performed extremely well, with high sensitivity, specificity, and positive and negative predictive value (96%, 100%, 100%, and 98%, respectively; Table 4), and high area under the ROC curve (0.9975; Figure 4). Protein:creatinine ratio had reasonable sensitivity (89%) but lacked specificity (49%), with a correspondingly lower area under the ROC curve (0.8770; Figure 5).

TABLE 4
Performance characteristics of 12-hour urine protein >165 mg and protein:creatinine ratio >0.15[a]

Variable[b]	Sensitivity	Specificity	Positive predictive value	Negative predictive value
12-hr urine protein of >165 mg	96 (90–99)	100 (96–100)[c]	100 (96–100)[c]	98 (93–100)
Protein:creatinine ratio	89 (81–94)	49 (39–59)	32 (23–42)	91 (84–96)

CI, confidence interval.

[a] A performance to predict 24-hour urine protein ≥300 mg; [b] Data are in percentage (95% CI); [c] 97.5% CI.

Tun. Twelve-hour urine protein and PCR vs 24-hour urine protein. Am J Obstet Gynecol 2012.

Comment

Our data suggest that both the 12-hour urine protein >165 mg and a protein:creatinine ratio >0.15 correlate significantly with 24-hour urine protein ≥300 mg in women with suspected preeclampsia. Several studies have suggested various cutoffs for the 12-hour urine protein and protein:creatinine.[5-8] To our knowledge, ours is the first to test these cutoffs prospectively.

In our study, a 12-hour urine protein >165 mg predicted 24-hour urine protein with high sensitivity and specificity (96% and 100%, respectively), which suggests that it is an appropriate surrogate for the 24-hour urine for the diagnosis of preeclampsia, with the potential for earlier diagnosis and treatment. Given the considerable maternal and neonatal morbidity that is associated with preeclampsia, an earlier diagnosis theoretically may decrease maternal and neonatal complications. Furthermore, for patients who ultimately are not given the diagnosis of preeclampsia (which was most of the women in our study), a shorter inpatient evaluation period would theoretically decrease cost by decreasing hospital stay by shortening the collection period. Finally, the shorter collection period may improve patient compliance with the collection (primarily in the outpatient setting) and improve accuracy.

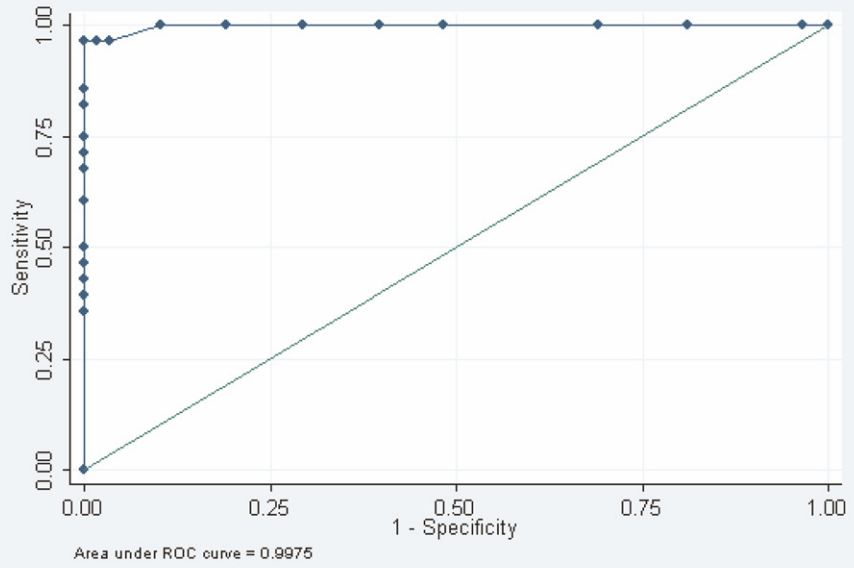
Although a protein:creatinine ratio >0.15 did not achieve the same level of sensitivity and specificity as 12-hour urine protein in our study for the prediction of 24-hour urine protein ≥300 mg, its high negative predictive value (91%) suggests that the best use of the protein:creatinine ratio may be to identify women who are unlikely to have a 24-hour urine protein ≥300 mg. It can be difficult to predict at the time of presentation which women with elevated blood

pressures will have a 24-hour urine protein ≥300 mg. In our cohort, for example, there were few differences in baseline characteristics at the time of admission between women who ultimately would or would not have ≥300 mg of protein in the 24-hour urine protein collection, including demographics, comorbidities (except pregestational diabetes mellitus), and admission blood pressure. Use of the protein:creatinine ratio therefore may be particularly useful in triaging women with mildly elevated blood pressure and to help decide where (inpatient vs outpatient) or when to do a timed urine collection for the evaluation of urine protein. Like the use of the 12-hour urine protein that was described earlier, this may also decrease cost by decreasing the frequency of admission and certainly would improve compliance and accuracy because no collection by the patient would be necessary. In addition, the cost of protein:creatinine ratio in our laboratory is roughly one-half that of a 12-hour or 24-hour collection ($17.26 vs $39.81). However, a full cost analysis was beyond the scope of our analysis.

Several previous studies have explored possible cutoff points for shorter urine collection periods.[5-7] We chose a cutoff of 165 mg for the 12-hour urine protein because it was generated from the (previously) largest available study that had evaluated 12-hour urine protein for the prediction of 24-hour urine protein ≥300 mg with good performance (83% sensitivity, 100% specificity, 100% positive predictive value, and 74% negative predictive value).[6] In our study, 12-hour urine protein >165mg performed even better than predicted by Adelberg et al[6] (Table 4).

Because of the increasingly popular use of protein:creatinine ratio to quantify proteinuria in nonpregnant patients and the convenience of the use of a spot urine over a timed collection, recent years have shown an increasing number of studies evaluating protein:creatinine ratio for the diagnosis of preeclampsia. However, there is less consensus in the literature and less consistency of findings than with the 12-hour urine protein. For example, values of 0.13 to 1.14 have been suggested[8,9]; therefore, the decision about which cutoff to evaluate in our study was not clear. We chose 0.15 as our cutoff to maximize sensitivity and to avoid the consequences of missing a patient who is likely to have preeclampsia. Our results were similar to other studies that have explored lower protein:creatinine ratio cutoffs,[8] although not quite as good as those described by Schubert et al (sensitivity 100%, specificity 50%, posi-

FIGURE 4
ROC for 12-hour urine protein



ROC, receiver operating characteristic.

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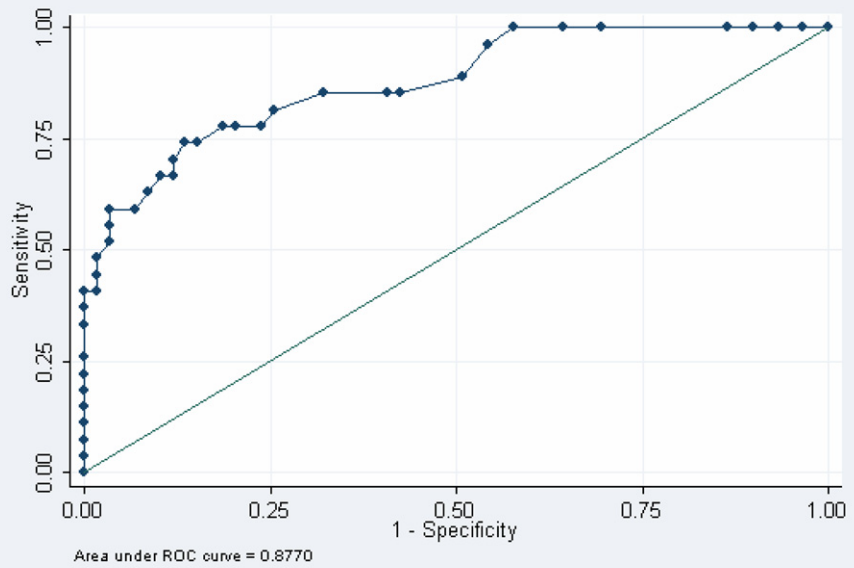
FIGURE 5
ROC for protein:creatinine ratio



ROC, receiver operating characteristic.

Tun. Twelve-hour urine protein and PCR vs 24-hour urine protein. Am J Obstet Gynecol 2012.

tive predictive value 75% and negative predictive value 100%),[7] which is not unexpected in a prospective evaluation of a cutoff. As suggested in 1 systematic review,[8] there may be value in the use of 2 cutoffs for protein:creatinine ratio (a lower cutoff with a high negative predictive value and a higher cutoff with a high positive predictive value) to identify patients who are so likely to have a 24-hour urine protein <300 mg and ≥300 mg, respectively, so that further evaluation is not necessary, which would save both time and cost. Secondary analysis of our data identifies a protein:creatinine ratio > 0.5 as a potential cutoff for the reliable prediction of a 24-hour urine protein ≥300 mg, with a positive predictive value of 100% (96-100%; 97.5% confidence interval). This cutoff must be validated prospectively in future studies.

Strengths of our study include "real life" study design that should be generalizable to clinical practice, such as starting the collection at the time of admission regardless of time of day. In addition, the inpatient setting insured consistency and compliance with the collection technique. By evaluating only inpatients, however, we may have limited our generalizability because of the uncertain impact of hospitalization on the results (diet, sleep pattern, activity level, compliance with collection). In addition, our study population was primarily white subjects, hence these tests may perform differently in a different population. Another limitation, like most studies on preeclampsia, is that our sample size did not allow us to correlate different tests with maternal and neonatal outcomes, which is ultimately what is most important. Finally, the positive and negative predictive values will vary with the prevalence of disease in a given population; therefore, these results cannot be generalized to a population with a significantly different prevalence of 24-hour urine protein ≥300 mg.

In summary, both 12-hour urine protein >165 mg and protein:creatinine ratio >0.15 appear to be useful tools for the prediction of 24-hour urine protein ≥300 mg with the potential benefits of earlier diagnosis and treatment of preeclampsia and perhaps decreased cost. Future studies should focus on the development and prospective evaluation of a clinical algorithm that would incorporate both of these tools for the evaluations of patients with suspected preeclampsia (both inpatient and outpatient), and ideally would correlate results with maternal and neonatal outcomes.

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