Original Research Article

Comparison of single spot urinary albumin-creatinine ratio with 24-hour urinary protein excretion in women with preeclampsia

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ABSTRACT

Background: The measurement of albumin: creatinine ratio (ACR) in a spot urine sample avoids the influence of variation in urinary solute concentration and provides a more convenient and rapid method to assess protein excretion. The aim of this study was to evaluate urinary spot ACR as a new marker for proteinuria and to study its correlation and accuracy in comparison with 24-hour urinary protein.

Methods: The prospective one-year study was conducted on 100 pregnant women, 18-40 years, >20 weeks gestation with a diagnosis of preeclampsia. A spot midstream urine sample was taken for detection of albuminuria by dipstick method. Another spot sample was taken for detection and calculation of spot ACR. The 24-hour urine collection was taken immediately afterward to evaluate 24-hour urinary protein excretion.

Results: A positive linear relation exists between ACR and 24-hour urinary protein excretion The ROC revealed cut-off of 20.4 with 88.5% sensitivity, 75% specificity, 98.8% positive predictive value and 21.4% negative predictive value. Spot urinary ACR >20.4 correctly identified women having 24-hour urinary protein excretion in excess of 0.3 gm/DL.

Conclusions: A strong correlation exists between single spot urinary ACR with 24-hour urinary protein excretion in women with preeclampsia.

Keywords: 24-hour urinary protein excretion, Albumin-creatinine ratio, Preeclampsia

INTRODUCTION

Hypertensive disorders are frequently encountered complications in pregnancies and are associated with increased risk of both adverse maternal and fetal outcome. Overall 10-15% of maternal death are directly associated with preeclampsia and eclampsia.[1]

Preeclampsia is a disorder of widespread vascular endothelial dysfunction and vasospasm that occur after 20 weeks of gestation and can present as late as 4-6 week postpartum.[2] The etiology of preeclampsia is unknown but thought to be related to hypoxia in the placenta due to abnormal placentation. Mild preeclampsia occurs in approximately 15% of pregnancies and severe in 1-2%.[3] It complicates 10% of pregnancies in developing countries and responsible for about 76000 maternal deaths every year.[4,5]

Minimum criteria for preeclampsia include blood pressure >140/90 mm Hg after 20 weeks gestation, proteinuria >300 mg/24 hours or >1+ dipstick.[2]

The measurement of protein excretion in a 24-hour urine collection is used as gold standard for the diagnosis and follow-up of pathological urinary excretion. However, the standard practice of collecting a 24-hour urine for a protein is cumbersome, time consuming and inconvenient

and only some women can have managed as outpatients and collect a 24-hr urine sample.[6] The dipstick analysis, using visual reagent strips, is quick, portable and easy to do but the test has relatively high false positive and false negative rate.[7] Spot urinary ACR overcomes these false positive and false negative rates.[6] The measurement of ACR in a spot urine sample avoids the influence of variation in urinary solute concentration and provide a more convenient and rapid method to asses protein excretion. Several international organizations have accepted the spot urine ACR as a reasonable method for the identification of significant proteinuria (>0.3g/24h) during pregnancy.[8-10]

METHODS

The present study was conducted on pregnant women attending outpatient department or admitted in Department of Obstetrics and Gynaecology, Government Medical College Jammu for a period of one year (October 2014 to September 2015). A total of 100 patients were selected according to inclusion criteria (18-40yrs of age, >20 weeks gestation) and excluding women with known kidney disease, connective tissue disorders, pre-existing diabetes, gestation diabetes and bacteriuria.

The patients were subjected to detailed history and clinical examination including general physical, Obstetrical and systemic examination. All the investigation including haemoglobin, bleeding time, clotting time, routine urine examination, prothrombin time, PTI, platelet count, renal function test, liver function test and urine for albumin, urine for creatinine, 24-hour urinary protein excretion and spot urinary ACR were noted down.

A spot midstream urine sample was taken for detection of albuminuria by dipstick method. Another spot sample was taken for detection and calculation of spot ACR. The 24-hour urine collection was taken immediately afterward to evaluate 24-hour urinary protein excretion. Only one 24-hr urine collection per women was included in the analysis.

The data was analysed using statistical software MS Excel and SPSS 17.0 for window. Correlation was assessed by Pearson method. Correlation coefficient and regression equation calculated using least square method. Scatter diagram was used to display the relationship between single spot urinary ACR and 24 hr urinary protein excretion. ROC curve was drawn and area under curve calculated.

RESULTS

A total of 100 patients were studied based on inclusion and exclusion criteria for a period of one year and following observations were made, mean age of patient with preeclampsia was 26.71 ± 3. Overall, 87% patient had mild preeclampsia (SBP/DBP; >140/>90mm Hg), 13% had severe preeclampsia (SBP/DBP; >160/>110mm Hg).

When mean spot urinary albumin level, mean spot urinary creatinine level, mean 24-hour urinary protein excretion level and mean spot urinary ACR were compared between patients with mild (n = 87) and severe preeclampsia (n = 13), the study found significantly higher level of mean albumin level, mean 24-hr protein excretion level and mean spot urinary ACR in patients with severe preeclampsia (Table 1).

Table 1: Comparison between patients with mild and severe preeclampsia.

Variable	Mild Pre-eclampsia (n = 87)	Severe Pre-eclampsia (n= 13)	Statistical Inference (Student s t- test)
Spot urinary albumin (mg/dL) (Mean±Standard deviation)	192.05±120.75	759.4±235.09	t = 13.64 / p = 0.0001
Spot urinary creatinine (mmol/dL) (Mean±Standard deviation)	5.27±1.14	5.30±0.96	t = 0.09 / p = 0.92
24-hour urinary protein excretion (g/L) (Mean±Standard deviation)	0.40±0.22	3.36±2.00	t = 13.64 / p = 0.0001
Spot urinary albumin creatinine ratio (mg/mmol) (Mean±Standard deviation)	36.35±21.34	140.56±32.72	t = 15.21 / p = 0.0001

Figure 1 shows that a positive linear relation exists between ACR and 24-hr urinary protein excretion. The correlation can be classified as very strong as evident by Pearson Coefficient r as 0.836. The coefficient of determination i.e. $R^2 = 0.70$ which means that 70% of the variation in one variable can be explained by another.

The regression equation could be written as y = a+bx or 0.484 + 0.26 x, where y denotes the dependent variable (24-hr urinary protein excretion) a as a intercept or change in y when x = 0 and b being regression coefficient (change in unit y given change per unit x)

The receiver operating characteristic curve analysis reveal cut-off as 20.4. A cut-off of 20.4 seems best trade-off between sensitivity 88.5% (80.6-93.4%) and specificity 75% (30-95.4%). The area under curve is 0.836 with confidence interval (CI, 0.64-1.00), which is indicative of excellent discriminating capability of the cut-off. Positive predictive value is 98% (93.7-99.7%), negative predictive value is 21.4% (7.57-47.5%), Likelihood ratio (positive) is 3.54 (0.49-25.2%). Likelihood ratio (negative) is 0.15 (0.10-0.22%) (Table2).

Table 2: Predictive index for albumin creatinine ratio for 0.3 gm/24 hour of protein excretion.

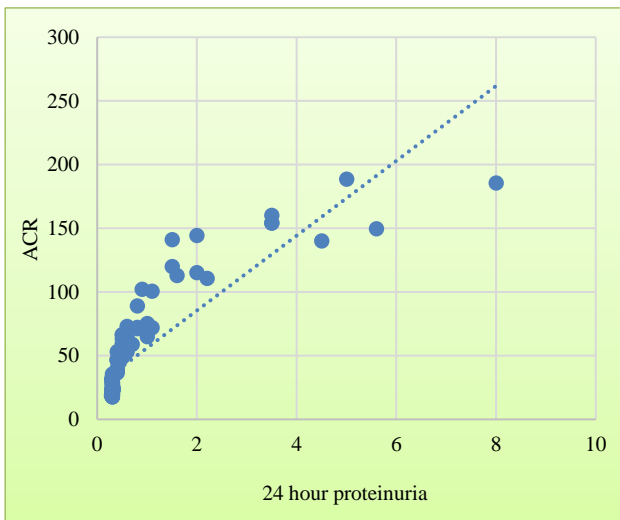| Variable	AUC (95% CI)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	LR+	LR-	Accuracy (%)
Spot urinary ACR	0.836 (O.64-1.00)	88.5	75	98.8	21.4	3.5	0.15	88

Figure 1: Scatter diagram showing correlation between spot urinary albumin creatinine ratio (ACR) and 24-hour urinary protein excretion.

Table 3 shows that spot urinary ACR correctly identifies majority of women having 24-hr urinary protein excretion in excess of 0.3gm/L and therefore can be gainfully used as a screening test.

Table 3: Accuracy and ability of spot urinary albumin creatinine ratio in predicting 24-hour urinary protein excretion.

Spot urinary albumin-creatinine ratio	24 hours urinary protein excretion		Total
	≥0.3 gm/L	< 0.3 gm/L	
≥20.4	85	1	86
<20.4	11	3	14
Total	96	4	100

The clinician can be quite confident in predicting that the patient has urinary protein excretion in excess of 0.3gm/L if the test is reported positive i.e spot urinary ACR is more than 20.4. In other words, the likelihood of women having urinary protein excretion in excess of 0.3gm/L is 3.5 times higher if test is positive than when it is negative.

DISCUSSION

As per Moiety et al, the mean spot urinary albumin level in 50 patients with severe preeclampsia was 3976.97±5580.22 mg/L and in 50 patients with mild preeclampsia was 717.99±1273.03 mg/L with p = 0.001 which is not consistent with the present study.[11] Huang et al reported mean spot urinary creatinine levels in patients with mild preeclampsia to be 51.8±8.97 mmol/L and 77.7±59.4 mmol/L in severe preeclampsia, which is similar to the present study.[12] Present result are consistent with Gao et al where 24 hours urinary protein excretion levels in mild and severe preeclampsia was 700±160 mg and 4800±2200 mg respectively with p<0.05.[13] As per Aggarwal et al the mean protein excretion was 1.33 g/L, which is consistent with the present study.[14]

As per Huang et al the mean standard deviation of spot urinary ACR levels in patient with mild preeclampsia was 72.68±12.4 mg/mmol as compared to that in patient with severe preeclampsia 401.2±345.1 mg/mmol respectively (p<0.05) which is not consistent with the present study.[12] The reason for this very high value can be the higher proportion of severe preeclampsia patients in their sample.

Our study is consistent with Ray et al with r = 0.94 and p<0.0001 and Al et al, with a cut-off protein creatinine ratio greater than 0.19 or 21 mg/mmol as a predictor of significant proteinuria, sensitivity and specifity were 85% and 73% respectively.[15,17] Positive and negative predictive value of the test were 46% and 95% respectively.

Our result are also consistent with Huang et al, optimal spot ACR cut-off point was 22.8 mg/mmol for 0.3g/24 hour of protein excretion (mild preeclampsia) with a

sensitivity and specify of 82.4% and 99.4% respectively and 155.6 mg/mmol for 2 g/24 hour of protein excretion (severe preeclampsia) with a sensitivity and specify of 90.6% and 99,6% respectively.[12] Cut-off of the present study is almost similar with that of Wilkinson et al, the authors concluded that both PCR and ACR are good rule out tests for significant proteinuria in pregnancy using cut-off point of <20 mg/mmol and <2.5 mg/mmol.[18]

In another study by Nisell et al, the optimal cut-off of ACR value of 27 mg/mmol the sensitivity, specificity, positive and negative predictive value for detecting albuminuria >300 mg/24 hour were: 95,100,100 and 86% respectively which is comparable with the present study.[19] In another study by Heerspink et al, spot urinary micro ACR cut-off of >30 mg/g (3.4 mg/mmol) is considered as positive for significant proteinuria and correlate well with 24-hour urine protein with sensitivity of 94% and specify of 98%.[20]

Cut-off of our study did not correlate with Moiety et al.[11] cut-off value for ACR for this group of patients was calculated to be 14.65 mg/mmol, above which severity of disease was highly probable. The sensitivity and specify were 100% and 58% respectively. The positive predictive value was 70.4% and negative predictive value was 100%. Cut-off of the present study also did not correlate with the threshold of Lamontagne et al, the study concluded that protein creatinine ratio threshold of 30mg/mmol reliably identifies significant proteinuria, but its reliability is reduced in first morning samples.[16] The median of protein to creatinine ratio in this study was 24 mg/mmol (range 0 to 108).

The cut-off in the present study was lower than that reported in other studies. The underlying reason for lower cut-off may be because of higher proportion of patients with mild preeclampsia (87%). This could also be due to different physiological reasons such as patients' hydration status, sample contamination with vaginal secretion and/or blood, infection, pH and specific gravity could contribute to the deviation of the result.

CONCLUSION

The study concludes that the gold standard 24-hour urinary assessment of albuminuria in preeclamptic women can be substituted with a single spot urinary ACR.

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