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Diagnostic accuracy of spot albumin creatinine ratio and its association with neonatal and maternal outcome in preeclampsia: Prospective analysis at a rural tertiary care centre

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Abstract
Spot urinary ACR detection of proteinuria has been recommended to screen pre-eclampsia during pregnancy.
Objective: Assessment of diagnostic accuracy of spot ACR and its association with neonatal and maternal outcome in preeclampsia.
Methods: Eighty pregnant women who reported to the antenatal OPD at 17-20 weeks of period of gestation were enrolled in the study over the period of one year from Jan 2018 to Dec 2018 at Department of Obstetrics & Gynaecology Dr Rajendra Prasad Govt. Medical College, Kangra at Tanda, Himachal Pradesh, India. Preeclampsia was defined as per NHBPEP2000 working group, resting hypertension >140/90 mmHg after 20th weeks of pregnancy.
Results: Prevalence of pre-eclampsia was 10%. Women with pre-eclampsia were significantly older than normotensive women (P=0.014). Incidence of pedal edema and abdominal edema was significant higher in the women with pre-eclampsia (P<0.05). 75% of pre-eclampsia women delivered neonates with low birth weight (P=0.044). Spot ACR was significantly higher in the women with pre-eclampsia in comparison to normotensive women (0.4 [0.22, 2.1] vs. 0.12 [0.1, 0.3]; P=0.003). Cut-off of spot ACR (>0.3), sensitivity and specificity were 62.5% and 79.2% while positive predictive value and negative predictive value were 25% and 90%. Diagnostic accuracy of spot ACR for detection of pre-eclampsia was 77.5%.
Conclusion: ACR could be very useful test for predicting the development of preeclampsia, maternal as well as neonatal outcomes.

Keywords: Urine albumin to creatinine ratio, pre-eclampsia, proteinuria

Introduction
Hypertensive disorders in pregnancy are one of the leading causes of maternal as well as perinatal morbidity and mortality globally. It complicates up to 10% of pregnancies [1]. Incidence of these disorders has increased by 25% in the United States during the past two decades[2] and estimated maternal deaths are between 50,000 and 60,000 every year worldwide [3, 4]. Proteinuria is one of the common and important features of preeclampsia. Proteinuria ≥300 mg/24 h urine collection or Dipstick reading of 1+ leads to diagnosis of preeclampsia. However, recent modified recommendations state non-essentiality of the component for the diagnosis of preeclampsia [1].
Urine dipstick method is a semi-quantitative colorimetric test. It is inexpensive, easily available and simple to do. It is very commonly performed test for screening of proteinuria, but it should be used only if other quantitative methods are not available [1]. It has high false positive rate, so it is always followed by other quantitative test [5]. Quantification of proteinuria can be done by other methods like 24 h urine collection and protein estimation. This is the traditional method and considered as Gold standard, but it has many drawbacks. It is time-consuming, inconvenient, and inaccurate because of over or under collection of urine [6].
Protein to creatinine (PC) ratio is a rapid, accurate, and convenient method. A spot urine PC ratio > 0.7 mg protein/mg creatinine strongly suggests a significant proteinuria [1].
Albumin-creatinine ratio (ACR) has the advantage of performing it using automated analyzer. Hence, this test is too rapid; results can be obtained on the same day [7-9].

Spot urine ACR based detection of proteinuria had been approved by several international organizations such as International Society for the Study of Hypertension in pregnancy [10], the Society of Obstetric Medicine of Australia and New Zealand [11], and the Society of Obstetricians and Gynaecologist of Canada [12, 13].

This study evaluated diagnostic accuracy of spot ACR and its association with neonatal and maternal outcome in preeclampsia.

Methods

Eighty pregnant women who reported to the antenatal OPD at 17-20 weeks of period of gestation and who fulfilled the inclusion criteria and were willing to participate in the study were enrolled in the study over the period of one year from Jan 2018 to Dec 2018 at Department of Obstetrics & Gynaecology Dr Rajendra Prasad Govt. Medical College, Kangra at Tanda, Himachal Pradesh, India.

Inclusion criteria included singleton pregnancy, gestation age between 17 and 20 weeks by last menstrual period verified by ultrasound, and normal renal function and no evident proteinuria upon measurement with a dipstick. Subjects with multi-fetal pregnancy, hematuria, dipstick-positive proteinuria, ongoing urinary tract infection, acute renal failure or chronic kidney disease, mental retardation or other mental disorders, gestation age below 17 or above 20 weeks by last menstrual period verified by ultrasound, lack of urine sample at the specified enrolment period, known major fetal anomaly or fetal demise, lack of demographic data, liver diseases, and/or history of present or past gout or use of diuretics, were excluded from the study.

Preeclampsia was defined as per NHBPEP2000 working group, resting hypertension >140/90 mmHg after 20th weeks of pregnancy.

Data analysis

Data were recorded into Microsoft® Excel 2019 and exported into SPSS. Quantitative data were expressed as median [interquartile range (IQR); Q1, Q3] and analysed using Mann-Whitney U test. Categorical variables were compared using Chi square test with or without Yate's correction. Receiver operating characteristic (ROC) curve analysis was used, and the area under the curve (AUC) was calculated. Sensitivity, specificity, and cut-offs for the were estimated using the 24-hour urinary protein excretion as the gold standard. *P* value <0.05 was considered significant. Statistical analysis was performed using SPSS v21.0.

Results

Maternal characteristics

In this study, prevalence of pre-eclampsia was 10%. We observed that women with pre-eclampsia were significantly older than normotensive women (*P*=0.014). None of the women with pre-eclampsia had gestational diabetes (*P*=0.709). Incidence of pedal edema and abdominal edema was significant higher in the women with pre-eclampsia (*P*<0.05). Pre-eclampsia was not associated with mode of delivery (*P*=0.869). Women with pre-eclampsia had lower Bishop Score than normotensive women; however, the difference was not statistically significant (*P*=0.364) (Table 1).

Table 1: Maternal characteristics

	Pre-eclampsia (n=8)	Normotensive (n=72)	*P* value
Age (years)	29.5 [28.2, 32.0]	27.0 [24.0, 29.0]	0.014
GDM, n	0	8	0.709
Pedal edema, n	5	3	0.035
Abdominal edema, n	1	2	0.019
Bishop score			
Mode of delivery (LSCS), n	20	3	0.869

Data expressed as median [IQR] otherwise expressed, GDM, gestational diabetes mellitus, LSCS, Lower segment caesarean section

Neonatal outcomes

Birth weight of neonates delivered through pre-eclamptic women had significantly lower birth weight in comparison to those delivered through normotensive women (*P*=0.029). We also observed that 75% of pre-eclampsia women delivered neonates with low birth weight (*P*=0.044). NICU admission and perinatal mortality were not associated with pre-eclampsia. There was no neonatal mortality in this study (Table 2).

Table 2: Neonatal outcomes

	Pre-eclampsia (n=8)	Normotensive (n=72)	*P* value
Birth weight (g)	2430 [2095.0, 2497.5]	2545.0 [2381.2.0, 2855.0]	0.029
Birth weight (<2500 g), n	6	23	0.044
NICU admission, n	1	2	0.695
Perinatal mortality, n	0	1	1.000
Neonatal mortality, n	0	0	-

Data expressed as median [IQR] otherwise expressed, NICU, neonatal intensive care unit

Spot ACR

In this study, we observed that spot ACR was significantly higher in the women with pre-eclampsia in comparison to normotensive women (0.4 [0.22, 2.1] vs. 0.12 [0.1, 0.3]; *P*=0.003) (Figure 1).

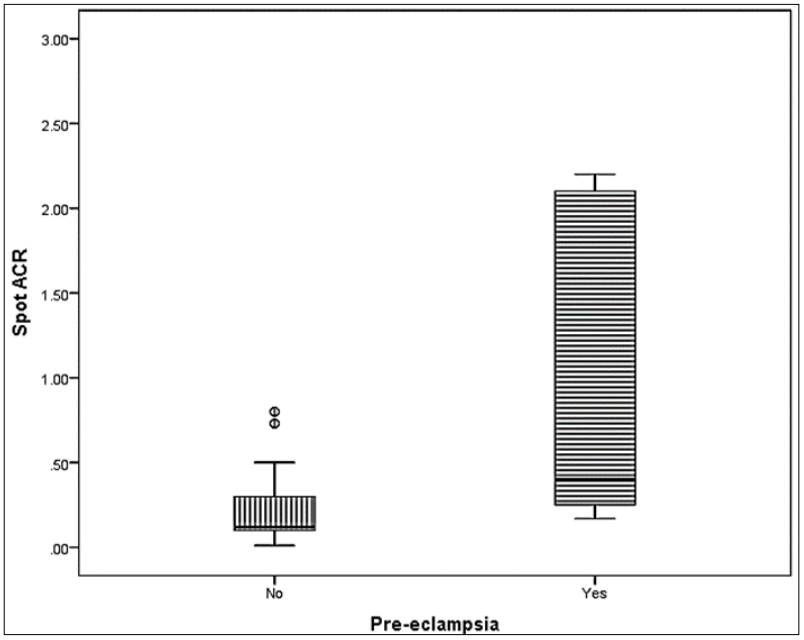

Fig 1: Boxplot showing comparison of spot ACR in pre-eclamptic and normotensive women

Diagnostic values

We observed that at the cut-off of spot ACR (>0.3), sensitivity and specificity were 62.5% and 79.2% while positive predictive value and negative predictive value were 25% and 90%. Diagnostic accuracy of spot ACR for detection of pre-eclampsia was 77.5%.

Receiver operative curve (ROC) characteristics

We measured area under the curve (AUC) based on the values of ACR in our study. We observed AUC of 0.819 with confidence interval (0.697-0.942). We also observed that at the cut-off of 0.22 of spot ACR, sensitivity and specificity were 75% and 72% respectively. ROC curve has been shown as figure 2.

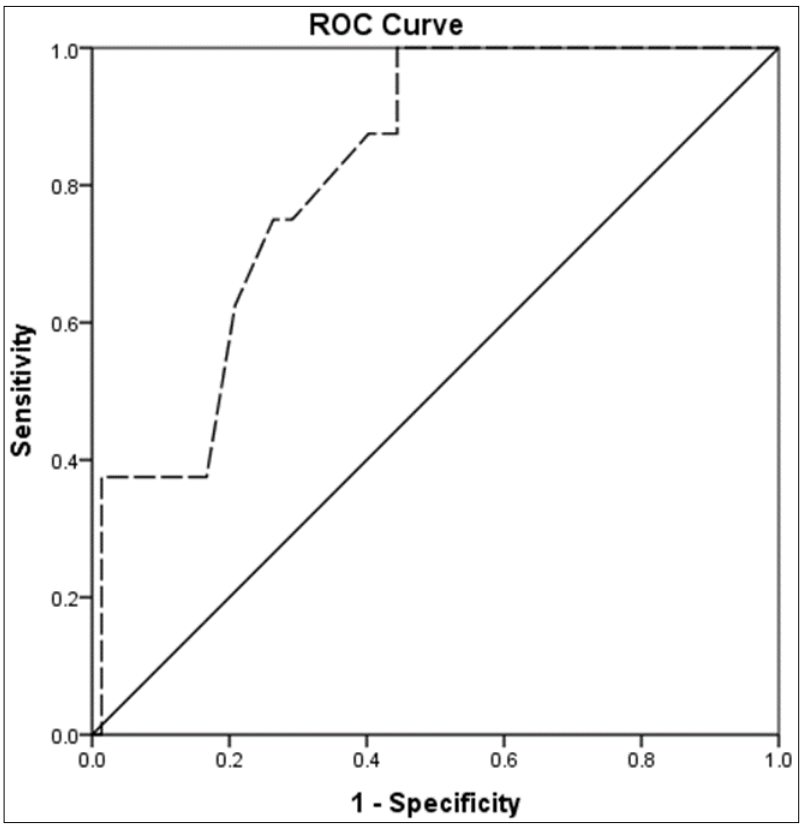

Fig 2: ROC characteristic

Discussion

Proteinuria is one of the diagnostic criteria of preeclampsia. The gold standard method of 24 hours urine protein estimation is cumbersome and time consuming. Dipstick method of evaluating proteinuria is not perfectly correlated. With negative to trace dipstick results; 66% women will have proteinuria > 300 mg in 24 hours. The protein to creatinine ratio of a single urine sample correlates significantly (P<0.001).

In this study, sensitivity and specificity were 62.5% and 79.2% while positive predictive value and negative predictive value

were 25% and 90%. Diagnostic accuracy of spot ACR for detection of pre-eclampsia was 77.5%. This is in accordance with previous studies. Robert *et al* [14], Rodrigues *et al* [15], Papanna *et al* [16] have shown high sensitivity, specificity and negative predictive value but in contrast to the low positive predictive value of the test (40%) detected in present study; they had shown a high positive predictive value for the test.

Huang *et al* [17] have shown that the optimal spot ACR cut off point was 22.8 mg/mmol for 0.3 g/24 h of protein excretion (mild preeclampsia) with a sensitivity and specificity of 82.4% and 99.4%, respectively, and 155.6 mg/mmol for 2 g/24 h of protein excretion (severe preeclampsia) with a sensitivity and specificity of 90.6% and 99.6%, respectively.

In conclusion, a spot ACR in might be considered for replacement of 24 h urine protein excretion in the evaluation of preeclampsia and eclampsia. This test also has the potential to replace urinary dipstick method in routine antenatal clinic, but more data are required. In our study, association of raised ACR values with adverse maternal as well as neonatal outcome was observed. However, limitation of our study is small sample size, so more studies with good sample size are required to validate these results. It appears that ACR could be very useful test in near future not only for predicting the development of preeclampsia, but it also predicts maternal as well as neonatal outcome.

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