

ORIGINAL RESEARCH

Diagnostic accuracy of spot urinary albumin to creatinine ratios for detection of significant proteinuria or adverse pregnancy outcome in patients with suspected pre-eclampsia: A prospective observational study

¹Dr. Deepika Sharma, ²Dr. Indu Kaul, ³Dr. B.R. Bhagat

¹Lecturer, ²Professor & Head(Retired), ³Associate Professor, Department of Obst & Gynae, SMGS, Jammu, Jammu & Kashmir, India

Corresponding author

Dr. Deepika Sharma

Lecturer, Department of Obst & Gynae, SMGS, Jammu, Jammu & Kashmir, India

Email: deepikash26@gmail.com

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ABSTRACT

Background: The albumin to creatinine ratio have been proposed as alternative methods for the assessment of proteinuria in pre-eclampsia, as they are simpler and more convenient than 24-hour urine collection. The present study has been objectively conducted to determine the diagnostic accuracy of albumin to creatinine ratio compared to 24 hour urine collection for the detection of significant proteinuria in patients with suspected pre-eclampsia, and their ability to predict adverse outcomes for mother and baby. **Methods:** The study was carried out at the Department of Obstetrics and Gynaecology at SMGS Hospital, Government Medical College, Jammu for a period of one year w.e.f October 2014 to September 2015. A total of 100 patients as per inclusion criteria of the study were included in the study after an approval was obtained from the Institute Ethics Committee. **Results:** The spot urinary albumin-creatinine ratio (ACR) had an AUC of 0.836 with a 95% CI of 0.64-1.00, indicating that it is a moderately good predictor of 0.3 gm/24 hour of protein excretion. The sensitivity was 88.5%, which suggests that the test can detect 88.5% of patients with 0.3 gm/24 hour of protein excretion. And the specificity ACR was 75%, indicating that the test can correctly identify 75% of patients without 0.3 gm/24 hour of protein excretion. **Conclusion:** The spot urinary albumin-creatinine ratio (ACR) is a useful tool in distinguishing between mild and severe preeclampsia, with a high statistical significance. It is a moderately good predictor of 0.3 gm/24 hour of protein excretion, with high sensitivity and specificity for correctly identifying patients with and without significant proteinuria.

Keywords: 24-hour urinary protein excretion, albumin-creatinine ratio, preeclampsia

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INTRODUCTION

Pre-eclampsia is a significant contributor to maternal and perinatal morbidity and mortality, occurring in 2-8% of pregnancies. This disease is characterized by multisystem endothelial dysfunction, resulting in glomeruloendotheliosis, which can lead to renal impairment and failure in severe cases.^[1-2] The diagnosis of pre-eclampsia is based on elevated blood pressure and significant proteinuria (≥ 0.3 g/24 hours) after the 20th week of gestation in previously normotensive and non-proteinuric patients.^[3]

Antenatal care includes a screening program that involves regular measurements of blood pressure and urinalysis for proteinuria, often using urinalysis dipsticks. However, dipstick analysis has high false positive and false negative rates and requires follow-up with the gold standard test of 24 hour urine collection, which is cumbersome, time-consuming, and subject to inaccuracies.^[4] The albumin to creatinine ratio have been proposed as alternative methods for the assessment of proteinuria in pre-eclampsia, as they are simpler and more convenient

than 24-hour urine collection. Some studies have shown that single spot ACR has a high sensitivity and specificity for detecting proteinuria in preeclampsia, while others have found that it underestimates the degree of proteinuria.^[5] This allows for a better understanding of the severity and progression of proteinuria in women with preeclampsia. To address this need for a rapid and accurate test to identify significant urinary proteinuria, the present study has been objectively conducted to determine the diagnostic accuracy of albumin to creatinine ratio compared to 24 hour urine collection for the detection of significant proteinuria in patients with suspected pre-eclampsia, and their ability to predict adverse outcomes for mother and baby.

METHODS

The study was conducted on pregnant women who were either attending the outpatient department or admitted to the Department of Obstetrics and Gynaecology at SMGS hospital Jammu, for a duration of one year, from October 2014 to September 2015. The inclusion criteria for the selection of the patients were as follows: age between 18-40 years and gestation period of more than 20 weeks. Women with known kidney disease, connective tissue disorders, pre-existing diabetes, gestational diabetes, and bacteriuria were excluded from the study. A total of 100 patients were selected based on these criteria. Detailed history and clinical examination,

including general physical, obstetrical, and systemic examination, were conducted on all patients. Investigations were carried out, including haemoglobin, bleeding time, clotting time, routine urine examination, prothrombin time, PTI, platelet count, renal function test, liver function test, and urine tests for albumin, creatinine, 24-hour urinary protein excretion, and spot urinary ACR. The results of these investigations were documented and analyzed using statistical software MS Excel and SPSS 17.

RESULTS

The study included 100 patients, with the majority falling within the age range of 26 to 30 years (47%) and the second most common age group being 21 to 25 years (35%). Patients below 20 years old comprised only 4%, while those aged 31 to 35 years accounted for 13%. Most of the patients (61%) had a weight in the range of 61-70 kg, while 29% had a weight in the range of 71-80 kg. The majority of patients (69%) were primigravida and nulliparous (72%). The number of live issues varied, with 73 patients having none and only a small percentage having multiple live issues. The study also revealed information on previous pregnancies and abortions. Out of 100 patients, 87 (87%) had SBP/DBP readings greater than 140/90 mmHg, indicating mild preeclampsia. The remaining 13 patients (13%) had SBP/DBP readings greater than 160/110 mmHg, indicating severe preeclampsia.

Table 1: Comparison of mean spot urinary albumin creatinine ratio (mg/mmol) between patients with mild and severe preeclampsia

Preeclampsia	Mean \pm standard deviation (mg/mmol)	Statistical inference (Student's t-test)
Mild preeclampsia (n=87)	36.35 \pm 21.34	t=15.21; p=0.0001*
Severe preeclampsia (n=13)	140.56 \pm 32.72	

Table 1, compares the mean spot urinary albumin creatinine ratio (mg/mmol) between patients with mild and severe preeclampsia. The table presents the number of patients in each group, along with the mean value and standard deviation of their spot urinary albumin creatinine ratio. The results indicate that patients with severe preeclampsia had a significantly higher mean spot urinary albumin creatinine ratio

(140.56 \pm 32.72 mg/mmol) compared to those with mild preeclampsia (36.35 \pm 21.34 mg/mmol) with a t-value of 15.21 and a p-value of 0.0001, indicating high statistical significance. The findings suggest that the spot urinary albumin creatinine ratio may be a useful tool in distinguishing between mild and severe preeclampsia.

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-
Spot Urinary ACR	0.836 (0.64-1.00)	88.5	75	98.8	21.4	3.5	0.15

The table 2 shows the predictive index for albumin-creatinine ratio for 0.3 gm/24 hour of protein excretion. The variables included are the area under the curve (AUC) with a 95% confidence interval (CI), sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), likelihood ratio positive (LR+), and likelihood ratio negative (LR-). According to the table, the spot urinary albumin-creatinine ratio (ACR) has an AUC of 0.836 with a 95% CI of 0.64-1.00, indicating that it is a

moderately good predictor of 0.3 gm/24 hour of protein excretion. The sensitivity is 88.5%, indicating that the test can detect 88.5% of patients with 0.3 gm/24 hour of protein excretion. The specificity is 75%, indicating that the test can correctly identify 75% of patients without 0.3 gm/24 hour of protein excretion. The PPV is 98.8%, indicating that the test has a high probability of correctly identifying patients with 0.3 gm/24 hour of protein excretion. The NPV is 21.4%, indicating that the test has a low probability of

correctly identifying patients without 0.3 gm/24 hour of protein excretion. The LR+ is 3.5, indicating that the test is useful in ruling in the diagnosis of 0.3

gm/24 hour of protein excretion. The LR- is 0.15, indicating that the test is not useful in ruling out the diagnosis of 0.3 gm/24 hour of protein excretion.

Table 3: Accuracy and ability of Spot Urinary Albumin-Creatinine Ratio in predicting 24 Hours 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

According to the table3, among the 86 patients with a spot urinary ACR greater than 20.4, 85 had a 24-hour urinary protein excretion greater than 0.3 gm/L and only 1 had a 24-hour urinary protein excretion less than 0.3 gm/L. On the other hand, among the 14 patients with a spot urinary ACR less than 20.4, 11 had a 24-hour urinary protein excretion greater than 0.3 gm/L and 3 had a 24-hour urinary protein excretion less than 0.3 gm/L

DISCUSSION

The present study was conducted to address an important clinical question related to the diagnosis and management of pre-eclampsia. Pre-eclampsia is a common complication of pregnancy and is associated with significant morbidity and mortality for both the mother and the baby. One of the key features of pre-eclampsia is proteinuria, which is traditionally assessed by 24-hour urine collection. However, 24-hour urine collection is time-consuming, cumbersome, and often inconvenient for patients, and can result in incomplete or inaccurate collection. The identification of "significant proteinuria" plays a crucial role in the diagnosis of pre-eclampsia, evaluation of perinatal risk, and management of hypertension in pregnant women. Women with significant proteinuria are at a heightened risk of maternal and perinatal morbidity and mortality. It is important to achieve an accurate diagnosis through reliable diagnostic tests to avoid inappropriate interventions such as unnecessary testing or treatment. In the United Kingdom, the standard protocol is for pregnant women to undergo a 24-hour urine collection for total protein estimation as an outpatient or an inpatient.¹ However, this method is inconvenient, costly, and can result in delayed diagnosis and treatment implementation. Additionally, it is prone to weaknesses such as incomplete collection and varying use of assays, leading to inconsistent test results. The albumin to creatinine ratio has been proposed as alternative methods for the assessment of proteinuria in pre-eclampsia, as they are simpler and more convenient than 24-hour urine collection. However, their diagnostic accuracy and ability to predict adverse outcomes for mother and baby have not been well-established. Therefore, the present study aimed to determine the diagnostic accuracy of the protein to creatinine ratio and albumin to creatinine ratio compared with 24-hour urine collection for the detection of significant proteinuria

in patients with suspected pre-eclampsia. The study evaluated the ability of these ratios to predict adverse outcomes for mother and baby, which could potentially lead to earlier detection and management of pre-eclampsia and improved outcomes for patients. In the present study, we included 100 patients, with most of them belonging to the age group of ((21 to 30) years old. Majority of them were primigravida and nulliparous, and had no live issues. Majority of patients had weight between 61-80 kg. About 87% had mild preeclampsia, while 13% had severe preeclampsia with high blood pressure readings. We observed that patients diagnosed with severe preeclampsia demonstrated a remarkably higher average of spot urinary albumin creatinine ratio (140.56 ± 32.72 mg/mmol) in comparison to those with mild preeclampsia (36.35 ± 21.34 mg/mmol), with a t-value of 15.21 and a p-value of 0.0001, indicating high statistical significance. These results suggest that the spot urinary albumin creatinine ratio may be a valuable tool in distinguishing between mild and severe preeclampsia.

Upon conducting receiver operating characteristic curve analysis, it was determined that a cut-off of 20.4 mg/mmol was the optimal threshold for the spot urinary albumin creatinine ratio. This value demonstrated an excellent discriminatory ability, with an area under the curve of 0.836 and a confidence interval of 0.64 to 1.00. Sensitivity and specificity were also notable, with 88.5% and 75%, respectively. Additionally, the positive predictive value was high at 98.8%, while the negative predictive value was lower at 21.4%. The likelihood ratio (positive) was 3.54 and the likelihood ratio (negative) was 0.15, indicating that the test accurately identifies women with urinary protein excretion above 0.3 gm/L. Our findings are consistent with previous studies such as Rodriguez-Thompson et al. (2001), Taherian et al. (2006), Al et al. (2004), and Wheeler et al. (2007), who reported similar cut-off values for albumin/creatinine ratio as predictors of significant proteinuria.^[6-9] Overall, our results suggest that spot urinary albumin creatinine ratio can serve as a reliable screening tool for identifying preeclampsia in pregnant women. Our study's results are also consistent with previous research. For instance; Huang et al. (2012) found an optimal spot ACR cut-off point of 22.8 mg/mmol for 0.3 g/24 hour 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 hour of protein excretion (severe preeclampsia) with a sensitivity and specificity of 90.6% and 99.6%, respectively.^[10] Our study's cut-off is nearly identical to Wilkinson et al.'s (2013) findings; they concluded that both PCR and ACR are effective rule-out tests for significant proteinuria in pregnancy, with cut-off points of <20 mg/mmol and <2.5 mg/mmol, respectively.^[11] Nisell et al. (2006) also found a comparable optimal cut-off of 27 mg/mmol for albumin/creatinine ratio in detecting albuminuria >300 mg/24 h, with a sensitivity, specificity, positive predictive value, and negative predictive value of 95%, 100%, 100%, and 86%, respectively.^[12] Heerspink et al. (2006) determined that a spot urinary microalbumin-creatinine ratio cut-off of >30mg/g (3.4mg/mmol) is positive for significant proteinuria and correlated well with 24-hour urine protein, with a sensitivity of 94% and specificity of 98%.^[13] However, our study's cut-off did not correlate with Kyle and Associates' (2008) threshold of >8.0 mg/mmol.^[14] The cut-off value obtained in our study was not consistent with that reported by Moiety et al. (2014), which determined a cut-off value of 14.65 mg/mmol for ACR in a similar patient cohort, above which the severity of the disease was highly probable. Their findings showed a sensitivity and specificity of 100% and 58.0%, respectively, with a positive predictive value of 70.4% and negative predictive value of 100%.^[15] Similarly, our results did not align with the threshold proposed by Lamontagne et al. (2014), who suggested a protein-to-creatinine ratio threshold of 30 mg/mmol for identifying significant proteinuria, albeit with reduced reliability in first morning samples. The median protein-to-creatinine ratio in their study was 24 mg/mmol (range 0 to 108).^[16] The observed lower cut-off value in our study could be attributed to a higher proportion of patients with mild preeclampsia (87%). Several physiological factors, such as hydration status, sample contamination with vaginal secretions and/or blood, infection, pH, and specific gravity, could also potentially contribute to deviation in the test results.

CONCLUSION

The spot urinary albumin-creatinine ratio (ACR) is a useful tool in distinguishing between mild and severe preeclampsia, with a high statistical significance. It is a moderately good predictor of 0.3 gm/24 hour of protein excretion, with high sensitivity and specificity for correctly identifying patients with and without significant proteinuria. However, the NPV is low, indicating that it may not be as useful in ruling out the diagnosis. Overall, the spot urinary ACR can be a helpful alternative to 24-hour urine collection for the assessment of proteinuria in patients with suspected pre-eclampsia, but additional studies are needed to confirm its diagnostic accuracy and ability to predict adverse outcomes for mother and baby.

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