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Original Research Article

# A PROSPECTIVE STUDY ON COMPARATIVE EFFICACY OF URINE PROTEIN CREATININE RATIO AND CALCIUM CREATININE RATIO IN DETERMINING ORGAN DYSFUNCTION IN ANTENATAL PATIENTS WITH PREECLAMPSIA

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## ABSTRACT

**Background:** Preeclampsia is a pregnancy-specific hypertensive disorder and a leading cause of maternal and perinatal morbidity. Early detection of organ dysfunction is critical, particularly in low-resource settings where access to complex investigations is limited. This study aimed to compare the usefulness of the urine protein–creatinine ratio (PCR) and urine calcium–creatinine ratio (CCR) in identifying maternal organ dysfunction among antenatal women with preeclampsia. **Materials and Methods:** This prospective study was conducted in the Department of Obstetrics and Gynaecology, K.A.P. Viswanatham Government Medical College, Tiruchirappalli. One hundred and fifty antenatal women with preeclampsia were enrolled and categorised into two equal groups based on urine PCR (≥0.3) and urine CCR (≤0.04). The primary outcome was maternal organ dysfunction involving renal, hepatic, neurological, or fundoscopic systems. Comparisons were performed using appropriate statistical tests and ROC analysis. **Results:** The mean maternal age was 25.3 ± 4.69 years, and 62% were primigravidae. Renal dysfunction was significantly more frequent in the CCR group (20%) than in the PCR group (5.3%) ($p = 0.007$). Fundoscopic abnormalities (25.3%) and neurological involvement (41.3%) were more frequent in the CCR group ($p < 0.001$). Liver dysfunction showed no significant difference between groups ($p = 0.623$). Urine CCR demonstrated higher sensitivity (75%) and diagnostic accuracy (71.3%), while urine PCR showed high specificity (95.65%) but low sensitivity. ROC analysis showed significantly higher diagnostic performance for CCR ($p < 0.001$). **Conclusion:** Urine CCR is a more sensitive marker than PCR for detecting maternal organ dysfunction in preeclampsia and may serve as a practical adjunctive screening tool in similar tertiary care and low-resource settings.

## INTRODUCTION

Preeclampsia is a significant obstetric complication and a leading to maternal and perinatal morbidity and mortality globally. It is a pregnancy-specific hypertensive disorder defined by the onset of hypertension after 20 weeks of gestation.1,2 On a global scale, preeclampsia is estimated to be responsible for > 50,000 maternal deaths and over 500,000 foetal deaths annually. The burden of preeclampsia is higher in developing countries, including India, with reported incidence rates up to more than developed countries.3 Many women with mild to moderate disease remain asymptomatic, leading to delayed diagnosis and challenges in early risk identification.4 Inadequately controlled preeclampsia can cause serious maternal complications such as renal, hepatic, and neurological involvement, by increasing maternal and perinatal mortality. A history of preeclampsia is associated with an increased long-term risk of cardiovascular diseases, including ischaemic heart disease, stroke, and thromboembolic events.2,3

A central pathological mechanism in preeclampsia is widespread endothelial dysfunction affecting the renal, cerebral, hepatic, and systemic vasculature. Endothelial injury reduces the availability of vasodilators, including nitric oxide, prostacyclin, and endothelium-derived hyperpolarising factor, while


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increasing vasoconstrictors such as endothelin-1 and thromboxane A2. This imbalance promotes vasoconstriction, hypertension, impaired tissue perfusion, and subsequent organ dysfunction.5

Various biochemical markers evaluated to assist in assessing disease severity and predicting complications. The urine calcium–creatinine ratio (CCR) shows hypocalciuria in preeclampsia, with lower values correlating with increasing disease severity. Previous studies have reported high specificity and negative predictive value for CCR, suggesting that it may be useful in the evaluation of preeclamptic women.6–8 The spot urine protein creatinine ratio (PCR) is a convenient alternative to 24-hour urine testing, with ≥ 0.3 indicating significant proteinuria. A systematic review indicates that the PCR showed good sensitivity, mainly when higher cut-off values are used, making it a practical method for assessing proteinuria.7,9,10

PCR has been reported to have higher specificity and positive predictive value than CCR in detecting renal, hepatic, and fundoscopic abnormalities.7 However, proteinuria alone does not reliably reflect the extent of multisystem involvement in preeclampsia, particularly in women with this disease. There is limited evidence directly comparing the urine PCR and CCR for identifying early maternal organ dysfunction rather than proteinuria alone. While both CCR and PCR have been studied independently, direct comparisons of their effectiveness in identifying organ dysfunction in women with preeclampsia are limited. Therefore, this study aims to compare the usefulness of the urine PCR and the CCR in assessing disease severity and organ dysfunction among antenatal women with preeclampsia.

Direct evidence comparing urine PCR and CCR for the early identification of maternal organ dysfunction, beyond the assessment of proteinuria alone, is limited. Both have been evaluated independently, comparative data to detect disease severity and organ involvement in preeclampsia are insufficient. Therefore, this study aims to evaluate biochemical parameters for assessing the severity of preeclampsia and to compare the efficacy of the urine PCR and CCR in identifying maternal organ dysfunction among antenatal women with preeclampsia.

## MATERIALS AND METHODS

This was a prospective observational comparative study conducted in the Department of Obstetrics and Gynaecology, K.A.P. Viswanatham Government Medical College and Mahatma Gandhi Memorial Government Hospital, Tiruchirappalli, a tertiary care teaching hospital for one year, from January 2024 to December 2024. The ethical committee was approved and written informed consent were obtained from all patients.

**Inclusion and exclusion criteria**

The study included antenatal women with singleton pregnancies of 20 weeks or more, previously normotensive and non-proteinuric, who developed blood pressure ≥140/90 mmHg on two occasions four hours apart. Women with chronic hypertension, pre-existing proteinuria, chronic kidney disease, liver dysfunction, molar pregnancy, or multiple gestations were excluded.

**Sample size**

The sample size was determined based on feasibility and comparability with previously published prospective comparative studies evaluating urine biomarkers in preeclampsia.

**Methods**

All antenatal women fulfilling the inclusion criteria and admitted during the study period were enrolled until the required sample size was achieved. Participants were classified into two groups based on spot urine analysis. Group 1 included women with a urine PCR ≥ 0.3, and Group 2 included women with a urine CCR ≤ 0.04.

Baseline data, including maternal age, obstetric history, gestational age at presentation, and blood pressure measurements, were recorded. Findings from the clinical examination were noted in detail. Each participant provided a single midstream spot urine sample, collected under aseptic conditions, for estimation of urinary protein, calcium, and creatinine, after which the respective ratios were calculated.

Venous blood samples were obtained to evaluate renal function through serum urea and creatinine levels and hepatic function through serum bilirubin, aspartate aminotransferase, and alanine aminotransferase measurements. Fundoscopic examination was performed to assess for hypertensive retinal changes. Neurological evaluation was undertaken in patients who showed relevant symptoms.

Renal, hepatic, fundoscopic, and neurological manifestations were analysed, and the diagnostic uses of both ratios were compared to determine their effectiveness in identifying organ dysfunction in preeclampsia. Renal dysfunction was defined by elevated serum urea or creatinine levels. Hepatic dysfunction was defined by elevated serum bilirubin or liver enzymes (AST, ALT). Neurological involvement was defined by clinical or radiological evidence such as seizures, PRES, or cerebrovascular events. Fundoscopic involvement was defined by hypertensive retinal changes on ophthalmological examination.

**Statistical analysis**

Data were analysed using SPSS version 29. Descriptive statistics were expressed as mean ± SD and percentages. Intergroup comparisons were performed using the independent t-test for continuous variables and the chi-square or Fisher's exact test for categorical variables. A p-value ≤ 0.05 was considered statistically significant. Diagnostic accuracy was evaluated using ROC analysis with comparison of AUCs by DeLong's test.


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## RESULTS

A total of 150 antenatal women with preeclampsia were enrolled and included in the final analysis. The mean age was 25.3 ± 4.69 years (range, 17–41). There were no exclusions or losses to follow-up after enrolment. The majority of participants were aged 18–25 years (81, 54%), and primigravidae constituted 93 cases (62%). Preterm gestation (<37 weeks) was observed in 86 women (57.33%). Overweight status was predominant, seen in 102 women (68%). Most participants had gestational weight gain <11 kg (88, 58.67%). [Table 1]

**Table 1: Baseline demographic and obstetric characteristics**

| Variable | Category | N (%) |
|---|---|---|
| Age (years) | ≤ 18 | 5 (3.33%) |
| | 18–25 | 81 (54%) |
| | 25–35 | 57 (38%) |
| | ≥ 35 | 7 (4.67%) |
| Gravida | Primigravida | 93 (62%) |
| | Multigravida | 57 (38%) |
| Gestational age | < 37 weeks | 86 (57.33%) |
| | ≥ 37 weeks | 64 (42.67%) |
| Body mass index (kg/m²) | Underweight (<18.5) | 10 (6.67%) |
| | Normal (18.5–24.9) | 31 (20.67%) |
| | Overweight (25–29.9) | 102 (68%) |
| | Obese (≥30) | 7 (4.67%) |
| Gestational weight gain | < 11 kg | 88 (58.67%) |
| | ≥ 11 kg | 62 (41.33%) |

Most women were either normotensive 77 (51.33%) or had mild preeclampsia 70 (46.67%), while severe preeclampsia was uncommon 3 (2%). Pedal oedema was present in most participants, predominantly graded as 1+ in 122 women (81.4%). Proteinuria was mainly graded as 1+ 66 (44%) or 2+ 57 (38%). Fundoscopy was normal in most participants 131 (87.3%). Neurological examination was normal in 118 women (78.7%). Posterior reversible encephalopathy syndrome was the most frequently observed neurological abnormality, occurring in 24 women (16%). No imminent complications were observed in 83 women (55.33%), while antepartum eclampsia was recorded in 17 women (11.33%). [Table 2]

**Table 2: Clinical profile and organ system involvement**

| Variable | Category | N (%) |
|---|---|---|
| Classification by systolic BP | Normotensive | 77 (51.33%) |
| | Mild preeclampsia (SBP 140–159 mmHg) | 70 (46.67%) |
| | Severe preeclampsia (SBP ≥160 mmHg) | 3 (2%) |
| Pedal oedema | 1+ | 122 (81.4%) |
| | 2+ | 20 (13.3%) |
| | Nil | 8 (5.3%) |
| Urine albumin | Trace | 18 (12%) |
| | 1+ | 66 (44%) |
| | 2+ | 57 (38%) |
| | 3+ | 9 (6%) |
| Fundoscopy findings | Normal | 131 (87.3%) |
| | Grade 1 retinopathy | 12 (8%) |
| | Grade 2 retinopathy | 4 (2.7%) |
| | Grade 3 hypertensive retinopathy | 1 (0.7%) |
| | Retinal detachment | 2 (1.3%) |
| Neurological findings | Normal | 118 (78.7%) |
| | PRES | 24 (16%) |
| | CVT | 2 (1.3%) |
| | CVT with infarct | 4 (2.7%) |
| | Extensive PRES | 1 (0.7%) |
| | Hypertensive leukoencephalopathy | 1 (0.7%) |
| Imminent sign | Nil | 83 (55.33%) |
| | Antepartum eclampsia | 17 (11.33%) |
| | Imminent eclampsia | 11 (7.33%) |
| | Severe preeclampsia | 9 (6%) |
| | HELLP syndrome | 8 (5.33%) |
| | Headache | 8 (5.33%) |
| | Acute kidney injury (AKI) | 6 (4%) |
| | Acute pulmonary oedema | 4 (2.67%) |
| | Epigastric pain | 3 (2%) |
| | Partial HELLP | 1 (0.67%) |


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Haemoglobin levels were comparable between the PCR group (10.95 ± 1.04 g/dL) and the CCR group (10.54 ± 1.09 g/dL), while platelet counts were markedly higher in the CCR group (8.35 ± 2.63 lakhs/mm³). Renal dysfunction was observed in 15 women (20%) in the CCR group compared with 4 women (5.3%) in the PCR group (p = 0.007). Fundoscopic abnormalities were present in 19 women (25.3%) in the CCR group, while none were observed in the PCR group (0%) (p < 0.001). Neurological abnormalities occurred in 31 women (41.3%) in the CCR group compared with 1 woman (1.3%) in the PCR group (p < 0.001). [Table 3]

**Table 3: Comparison of laboratory parameters and organ system dysfunction between groups**

| Parameter | | | Group 1: PCR ≥ 0.3 (n = 75) | Group 2: CCR ≤ 0.04 (n = 75) | P value |
|---|---|---|---|---|---|
| Haematological parameters | Haemoglobin (g/dL) | | 10.95 ± 1.04 | 10.54 ± 1.09 | - |
| | Platelet count (×10⁵/mm³) | | 2.61 ± 0.59 | 8.35 ± 2.63 | - |
| Organ system | Renal function tests | Urea (mg/dL) | 16.72 ± 3.26 | 20.21 ± 10.62 | - |
| | | Creatinine (mg/dL) | 0.64 ± 0.13 | 0.86 ± 0.54 | - |
| | Liver function tests | Serum bilirubin (mg/dL) | 0.46 ± 0.18 | 1.05 ± 2.13 | - |
| | | SGOT (U/L) | 15.03 ± 4.74 | 22.23 ± 2.14 | - |
| | | SGPT (U/L) | 12.90 ± 3.59 | 20.91 ± 2.40 | - |
| | | ALP (U/L) | 145.43 ± 5.32 | 173.51 ± 10.36 | - |
| | Liver function (LFT) | Normal | 36 (48%) | 32 (42.7%) | 0.623 |
| | | Deranged | 39 (52%) | 43 (57.3%) | |
| | Renal function (RFT) | Normal | 71 (94.7%) | 60 (80%) | 0.007 |
| | | Deranged | 4 (5.3%) | 15 (20%) | |
| | Fundoscopy | Normal | 75 (100%) | 56 (74.7%) | <0.001 |
| | | Abnormal | 0% | 19 (25.3%) | |
| | Neurological status | Normal | 74 (98.7%) | 44 (58.7%) | <0.001 |
| | | Abnormal | 1 (1.3%) | 31 (41.3%) | |

Urine CCR showed higher sensitivity (75%) and accuracy (71.33%) with significant diagnostic value (p < 0.001). Urine PCR showed high specificity (95.65%) but low sensitivity (31.73%) with no statistical significance (p = 0.06). [Table 4]

**Table 4: Diagnostic performance of urine PCR and CCR in predicting organ dysfunction**

| Diagnostic marker | Urine protein creatinine ratio (spot) | Urine calcium creatinine ratio (spot) |
|---|---|---|
| Cut-off value | ≥ 0.3 | ≤ 0.04 |
| Sensitivity (%) | 31.73 | 75 |
| Specificity (%) | 95.65 | 63.04 |
| PPV (%) | 94.29 | 82.11 |
| NPV (%) | 38.26 | 52.73 |
| Accuracy (%) | 51.33 | 71.33 |
| P value | 0.06 | <0.001 |

ROC analysis showed significant diagnostic performance for urine CCR (p < 0.001), while urine PCR was insignificant (p = 0.06). Pairwise comparison using DeLong's test showed a significant difference between CCR and PCR (p = 0.01). [Table 5]

**Table 5: ROC analysis and pairwise comparison of urine PCR and CCR for predicting organ dysfunction**

| Analysis type | Diagnostic test | p value |
|---|---|---|
| ROC analysis | Urine spot PCR | 0.06 |
| | Urine spot CCR | <0.001 |
| Pairwise comparison (DeLong's test) | Urine spot PCR vs urine spot CCR | 0.01 |

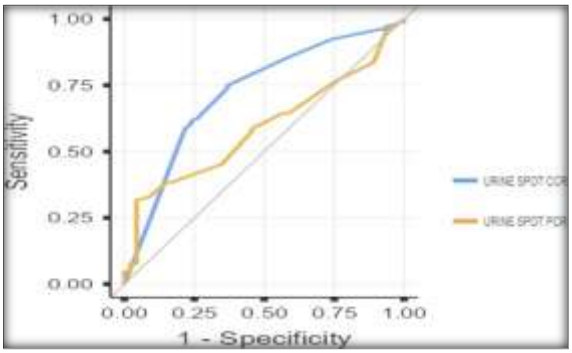


**Figure 1: ROC curve showing the diagnostic accuracy of urine spot PCR and CCR**

## DISCUSSION

This prospective study evaluated the urine PCR and CCR for detecting organ dysfunction in preeclampsia. the study included young, primigravid, overweight women, many presenting preterm with mild disease. A subclinical organ involvement was frequently observed. The CCR identified a higher prevalence of renal, neurological, and fundoscopic abnormalities than the PCR, while hepatic involvement was similar. Biochemical markers of renal dysfunction were higher in the CCR group,


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while hepatic involvement was comparable between groups.

In our study, participants were predominantly young primigravidae, frequently preterm at presentation, with a high prevalence of overweight status and lower gestational weight gain. Similarly, Mounika et al show a mean age of 23.5 ± 3.96 years, which was similar to our findings, with a minimum age of 18 years and a maximum age of 38 years, and the majority (53%) were primigravidae, while 30% were multigravidas.[11] Shao et al. found that pre-pregnancy overweight and excessive gestational weight gain increased preeclampsia risk, with overweight women showing significantly higher odds than normal-weight women.[12] These studies report similar young, primigravid cohorts and confirm that maternal overweight and gestational weight gain significantly increase preeclampsia risk, supporting our demographic and obstetric findings.

In our study, at presentation, most women had mild disease with frequent oedema, largely normal neurology, few complications, and antepartum eclampsia predominating. Similarly, Sharma et al. reported severe preeclampsia in 0.28% of 22,180 deliveries, confirming that severe presentations are relatively uncommon.[13] Iqbal Anvar et al. found that in preeclampsia/eclampsia, pedal oedema was in 74.2% of patients (52/70) from a retrospective clinical outcomes study.[14] Mukherjee et al. in a prospective cohort of severe preeclampsia/eclampsia, PRES occurred in 16.66% of patients (7/42).[15] Vennela et al. reported eclampsia in 11.6% (11/95) of PIH cases, while most women had no severe maternal complications.[16] These studies show predominantly mild preeclampsia, frequent oedema, low severe disease burden, comparable PRES rates, and eclampsia as the commonest adverse complication.

Our study shows haemoglobin was comparable between groups, but the CCR group showed higher renal, fundoscopic, and neurological involvement, indicating more subclinical organ dysfunction. Similarly, Sah et al. reported that severe preeclampsia showed significantly higher bilirubin, SGOT, SGPT, ALP, urea, creatinine, and uric acid ($p < 0.001$). Organ dysfunction increased with PIH severity, being more in the CCR group (LFT 70%, RFT 64.3%, fundus 84.6%) than the PCR group.[7] These findings support our study by showing that CCR better shows disease severity, identifying higher renal, hepatic, and fundoscopic involvement with subclinical organ dysfunction.

In our study, the urine CCR showed better sensitivity and overall diagnostic accuracy, while the urine PCR was highly specific but less sensitive for detecting organ dysfunction. In contrast, Sah et al demonstrated higher sensitivity and PPV for PCR as compared to CCR (92.3% and 86.05% vs 86% and 79%, respectively.[7] In another study by Mounika et al., the sensitivity and specificity of urine spot CCR were 58.3% and 64.5%, which were lower than those compared to our findings.[11] These studies highlight variability in marker performance, strengthening our finding that CCR may better detect subclinical organ dysfunction in our study population. These discrepancies may indicate differences in outcome definitions and disease spectrum at presentation.

Our study shows that ROC analysis confirmed the superior discriminatory ability of the urine CCR compared with PCR, supported by DeLong's method. In a study done by Rizk et al., PrCr predicted significant proteinuria (AUC 0.82, $p<0.001$), outperforming CaCr (AUC 0.55); a >0.19 cut-off gave 80.4% sensitivity and specificity 68.8%.[17] These findings evaluated the ability of PCR and CCR to predict significant proteinuria, rather than maternal organ dysfunction, which limits direct comparability with the outcomes assessed in the present study.

**Strengths**

Our prospective study, two groups, spot urine testing, comprehensive organ assessment, and ROC analysis showed superior CCR diagnostic performance in preeclampsia. Urine CCR allows early detection of subclinical organ dysfunction, timely guiding intervention and improving maternal outcomes in preeclampsia settings. CCR should be considered an adjunct to, rather than a replacement for existing laboratory assessment.

**Limitations**

This single-centre design limits generalisability, and the modest sample size restricts subgroup analysis. Longitudinal follow-up lack prevents assessment of disease progression. Multivariable adjustment absence may allow confounding by gestational age, body mass index, or treatment effects.

## CONCLUSION

Urine CCR showed higher sensitivity than urine PCR for detecting maternal organ dysfunction in preeclampsia. Renal, neurological, and fundoscopic involvement was identified even in mild cases. Urine PCR was highly specific but less effective for early detection. Urine CCR may be a useful adjunct in routine antenatal screening, especially in low-resource settings. Larger multicentre studies with longitudinal follow-up are needed to validate its role in early risk stratification.

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