TPM Vol. 32, No. S2, 2025
ISSN: 1972-6325
https://www.tpmap.org/

Open Access

ELEVATED SPOT URINE PROTEIN-CREATININE RATIO IN NORMOTENSIVE PREGNANCY: CLINICAL RELEVANCE AND THE ROLE OF CREATININE

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Abstract
Proteinuria is a widely recognized marker of renal dysfunction during pregnancy, particularly in the context of hypertensive disorders such as preeclampsia. However, elevated spot urine protein-to-creatinine ratio (PCR) is increasingly being detected even in normotensive pregnant women. This raises concerns about potential overdiagnosis and the risk of unnecessary interventions. The reliability of the PCR largely depends on the concentrations of both urinary protein and creatinine. Notably, fluctuations in urinary creatinine—affected by factors like maternal muscle mass, hydration status, and renal tubular function—can result in an overestimated ratio, even when actual protein excretion remains within normal physiological limits.[1,2]. This case series presents four pregnant women with elevated Spot PCR despite normal blood pressure, highlighting the diagnostic and prognostic challenges in such scenarios. Further research is warranted to refine the clinical utility of Spot PCR beyond hypertensive pregnancy disorders [3].

INTRODUCTION

Pregnancy is marked by intricate and dynamic immunological adaptations that are essential for supporting fetal development while preserving maternal immune defense. Disruption of these immunological balances can result in a spectrum of pregnancy complications, including hypertensive disorders such as preeclampsia, gestational diabetes mellitus (GDM), Fetal growth restriction (FGR), and preterm labor.[4,5]. Notably, autoimmune disorders, including systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS), have been implicated in adverse pregnancy outcomes due to persistent immune activation and complement dysregulation. The presence of autoantibodies such as anti-nuclear antibodies (ANA), anti-Ro/La, and anti-Jo-1 has been correlated with pregnancy complications [6]

The spot protein-to-creatinine ratio (PCR) has become a widely used, convenient tool in obstetric practice for estimating proteinuria in pregnancy. It offers an alternative to the traditional 24-hour urine collection, which, while accurate, is time-consuming, inconvenient for patients, and prone to collection errors. It provides a quicker assessment by comparing the amount of protein to creatinine in a single urine sample, ideally reflecting daily protein excretion.[7,8] This test is particularly valuable in screening for hypertensive disorders such as preeclampsia. However, its interpretation is not always straightforward. In pregnancy, physiological changes—such as increased renal blood flow, dilutional effects, and changes in muscle mass—can significantly influence creatinine excretion. When urinary creatinine is low, even a modest amount of protein can yield a disproportionately high PCR, leading to false-positive results. This is especially important in normotensive women, where elevated PCR may not reflect true pathology but rather normal pregnancy physiology or dilutional effects. As a result, clinical decisions should not rely solely on spot PCR values but consider the full clinical context, including blood pressure trends, symptomatology, and, when needed, confirmation through 24-hour urine testing. A balanced and cautious interpretation helps avoid unnecessary anxiety, overtreatment, or premature delivery in otherwise healthy pregnancies.Elevated Spot PCR values may indicate immune activation, necessitating multidisciplinary management [9]

In this case series, we present four pregnant women who underwent Spot PCR testing for various clinical indications, including autoimmune screening, suspected preeclampsia, GDM, and unexplained fetal growth concerns.

Case 1 involved a normotensive pregnant woman with elevated spot PCR (up to 2.41) but low serum creatinine (0.4 mg/dL) and normal 24-hour protein, suggesting a falsely elevated ratio. Concurrent UTI and positive anti-Jo-1 antibody further complicated interpretation.
Case 2 presented with bilateral pedal edema and acute gastroenteritis at 36 weeks, necessitating differential diagnosis for pre-eclampsia and infection-related inflammation. Case 3 involved a normotensive pregnant woman with well-controlled GDM
and borderline oligohydramnios, a condition linked to placental dysfunction and inflammatory pathways .
Case 4 involved a normotensive primigravida with transiently elevated spot PCR likely due to low urinary creatinine

Case presentation

Case 1: Concurrent UTI and Autoimmune Screening in Pregnancy

A G2P1L1 woman at 39 weeks + 3 days presented in spontaneous labor and delivered a healthy baby via normal vaginal delivery (NVD) with a right mediolateral episiotomy (RMLE). In this case, a normotensive woman exhibited repeatedly elevated spot protein-to-creatinine ratio (PCR), with values ranging from 1.2 to 2.41 across serial testing. However, her serum creatinine was notably low at 0.4 mg/dL, a physiological change common in late pregnancy due to increased glomerular filtration and reduced muscle mass. This low creatinine excretion contributed to an elevated PCR, raising concern for significant proteinuria, despite a normal 24-hour urinary protein excretion. Adding to the diagnostic complexity, her urine culture revealed Escherichia coli infection, which may have transiently increased urinary protein due to inflammation, while microscopy showed abundant WBCs and epithelial cells, consistent with urinary tract infection (UTI). Furthermore, she tested positive for anti-Jo-1 antibodies on ANA immunoblot, raising the possibility of an underlying autoimmune spectrum. Still, the absence of systemic features and stable clinical status suggested a subclinical immune response. Her elevated complement levels (C3 and C4) and normal serum albumin further reduced the likelihood of active glomerular disease. This case illustrates how low urinary creatinine and infection-related inflammation can both elevate the spot PCR in a normotensive pregnancy. It underscores the importance of interpreting PCR values in the broader context—considering serum creatinine, 24-hour protein, urinary tract health, and systemic immune markers—to avoid misclassification of renal pathology and unnecessary obstetric interventions.

Case 2: Acute Gastroenteritis with Pedal Edema

A primigravida at 36 weeks + 4 days was admitted with complaints of acute gastroenteritis and bilateral pedal edema (Grade 2). Despite initial concerns, her blood pressure remained within normal limits and urine dipstick did not show proteinuria, effectively ruling out preeclampsia. Lab investigations revealed mild dehydration, elevated white blood cell count, low albumin, and a serum creatinine of just 0.4 mg/dL—lower than typical pregnancy values. This low creatinine level is particularly relevant when interpreting the spot protein-to-creatinine ratio (PCR), which was 0.45. While this value may seem mildly elevated, it must be viewed in the context of her low urinary creatinine (15.9 mg/dL), which likely contributed to a deceptively higher PCR despite absent proteinuria and normal urinary findings on microscopy and culture. This highlights a common pitfall in assessing proteinuria using spot PCR alone—especially in normotensive women with concurrent dehydration , where urinary creatinine may be disproportionately reduced. Her symptoms resolved with fluid correction , and no evidence of renal or systemic pathology was found. This case underscores the need for cautious interpretation of spot PCR in pregnancy, particularly when urinary creatinine levels are low, as it may lead to overestimation of proteinuria and misclassification of risk.

Case 3: Gestational Diabetes Mellitus (GDM) & Borderline Oligohydramnios

A G2P1L1 woman at 34 weeks + 2 days with a history of previous lower segment cesarean section (LSCS) presented for routine antenatal follow-up. In this case she was gestational diabetes mellitus (GDM on MNT), borderline oligohydramnios, and no clinical signs of preeclampsia, an elevated spot urine protein-to-creatinine ratio (PCR) of 2.41 was noted. Interestingly, her 24-hour urinary protein was (614 mg/dl), and her blood pressure remained stable throughout, indicating a normotensive state. Calcium creatinine ratio was 0.1.

The disproportionate elevation of spot PCR despite normal BP and absent proteinuria on dipstick may be attributed to low urinary creatinine concentrations (0.4 mg/dL serum creatinine), likely influenced by physiological hemodilution, reduced muscle mass, or increased glomerular filtration during pregnancy. Furthermore, underlying autoimmune positivity (PM 100 on ANA blot) may also play a subtle role in altering glomerular permeability or renal handling of proteins. This highlights the importance of interpreting elevated spot PCR in context—especially in normotensive pregnancies where isolated PCR elevation could reflect altered creatinine excretion rather than true pathological proteinuria. Over-reliance on a single spot PCR may lead to unnecessary investigations or interventions; thus, 24-hour urine collection remains a valuable adjunct in these clinical scenarios. Preeclampsia is associated with abnormal calcium metabolism, possibly due to altered renal handling and increased calcium reabsorption. A low Ca:Cr ratio—typically <0.04 in spot urine—has been observed in many women who go on to develop preeclampsia. Because creatinine provides a stable baseline for this ratio, it enhances the test's sensitivity

and specificity. Hence, in normotensive women, a declining Ca:Cr ratio may act as a biochemical marker for impending preeclampsia, prompting closer monitoring and early intervention.

Case 4 :

A primigravida, 21 weeks presented with symptoms of headache and intermittent blurring of vision—features that often prompt evaluation for preeclampsia. However, her blood pressure was normal, and there was no clinical evidence of hypertension or proteinuria. Interestingly, her spot urine protein-to-creatinine ratio (PCR) showed variability, with an initial ratio of 0.63 and a repeat value of 0.06, despite consistently normal urine albumin and absence of proteinuria on dipstick. One notable finding was her low serum creatinine level (0.4 mg/dL), which may have contributed to the relatively elevated spot PCR in the absence of significant protein loss.

DISCUSSION

This case series highlights the utility of spot urine protein-to-creatinine ratio (Spot PCR) as a diagnostic tool in normotensive pregnancies complicated by diverse conditions, challenging its traditional association with hypertensive disorders such as preeclampsia.

Creatinine concentration in urine can be influenced by factors such as hydration status, muscle mass, and renal tubular function. In pregnancy—especially in young, lean women, vegetarian diet—low serum and urinary creatinine levels are common due to hemodilution [7,14] and increased glomerular filtration rate (GFR). When the urinary creatinine denominator is reduced, even normal or mildly elevated urinary protein can lead to a disproportionately high PCR value. This physiological shift, if not considered, can mimic early renal involvement or raise suspicion for hypertensive disorders, even in normotensive individuals.

This subtle but significant issue has been increasingly recognized in recent literature. Studies published between 2020 and 2025 have consistently shown that a notable proportion of normotensive pregnant women with elevated spot PCR—up to 15–20%—actually have normal 24-hour protein excretion. For instance, a 2022 study by Chatterjee et al. found that up to 20% of normotensive pregnant women with PCR >0.3 had normal 24-hour proteinuria, attributing the elevation partly to low urinary creatinine levels influenced by reduced muscle mass and hydration status [15]. Similarly, a 2021 analysis by Bano et al. emphasized that spot PCR may yield falsely elevated results in underweight women or those on vegetarian diets, reinforcing the need for careful interpretation [16]. Gupta et al. (2023), who highlighted the risk of overdiagnosis when PCR is interpreted in isolation.[17]. This discrepancy underscores the need for cautious interpretation of PCR values in isolation, particularly in women who do not exhibit clinical symptoms of preeclampsia or renal disease. To address this issue, several alternative approaches have been proposed. These include interpreting PCR results in conjunction with urinary creatinine levels or correcting for maternal body surface area. Some guidelines advocate for the use of 24-hour urine protein estimation, particularly when spot PCR values are borderline or when the clinical picture is incongruent [21]. Additionally, assessing trends over time, rather than relying on isolated PCR values, helps avoid misinterpretation and the risk of over-diagnosis.

Ultimately, elevated spot PCR in a normotensive pregnant woman is not always synonymous with renal pathology or preeclampsia. It is crucial to consider contributing physiological and biochemical factors—especially low urinary creatinine—before drawing conclusions. A comprehensive, context-driven approach to evaluation helps ensure that maternal anxiety is minimized, overtreatment is avoided, and clinical decisions are based on meaningful evidence rather than numerical artifacts.

CONCLUSION:

While the spot urine protein-to-creatinine ratio (PCR) remains a convenient and accessible screening tool in pregnancy, its interpretation must be approached with caution—particularly in normotensive women. Elevated PCR values in the absence of clinical symptoms or hypertension may not always reflect true pathological proteinuria, but rather result from disproportionately low urinary creatinine levels influenced by factors such as reduced muscle mass, hydration status, or dietary patterns. Overreliance on isolated PCR results can lead to unnecessary investigations, maternal anxiety, and even premature interventions. A more balanced approach that incorporates clinical context, repeat testing, and confirmation with 24-hour urine protein estimation where appropriate is essential. [22,23]. Recognizing these nuances ensures better-informed decisions and safeguards maternal and fetal well-being in pregnancies that might otherwise proceed normally.

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