

Comparison of Spot Urine Protein-Creatinine Ratio With 24-Hour Urine Protein in Women with Preeclampsia

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Author's Contribution

^{1,3}Substantial contributions to the conception or design of the work; or the acquisition, Active participation in active methodology, ²Drafting the work or revising it critically for important intellectual content, analysis, or interpretation of data for the work, ⁴Final approval of the study to be published

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ABSTRACT

Objective: To determine the diagnostic accuracy of spot protein creatinine ratio (sPCR) in predicting preeclampsia, taking 24 hours urinary protein as the gold standard.

Methodology: This descriptive analytical study was carried out at the Department of Obstetrics and Gynecology, Pakistan Institute of Medical Sciences, Islamabad from May 2021 to November 2021. The inclusion criteria were pregnant women with suspected preeclampsia, who were aged 20-40 years with singleton pregnancy and a gestational age >20 weeks. Patients having fulminant preeclampsia and those with associated comorbid conditions such as urinary tract infection, gestational diabetes mellitus, chronic hypertension, chronic liver disease and renal disease were excluded. All included women provided a 24-hour urine collection for determination of proteinuria. All women were advised to pass urine at 6:00 am and collect all the urine subsequently till 6:00 am the next morning (24-hour period). The adequacy of urine collection was determined by creatinine excretion. Urine sample for spot protein-creatinine ratio was collected the next morning after the 24-hour collection was over. Urinary protein quantitation was done by Biuret method, and urinary creatinine estimation was done by modified Jaffe's method.

Results: Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of protein creatinine ratio in predicting pre-eclampsia, taking 24 hours urinary protein as gold standard was 86.96%, 87.36%, 84.51%, 89.41% and 87.18% respectively.

Conclusion: The diagnostic accuracy of spot urine protein creatinine ratio in predicting preeclampsia was reasonably high. Hence we recommend it as the preliminary screening modality for diagnosing preeclampsia in our pregnant population. It is beneficial on the accounts of its being of economical, simple and fast.

Keywords: Preeclampsia, Spot protein creatinine ratio, 24 hours urine. Pregnancy.

Introduction

Preeclampsia, a common cause of maternal morbidity occurring in up to 2%-8% of all pregnancies.¹ It is a multisystem endothelial disease that leads to glomeruloendotheliosis and in severe cases it may lead to renal impairment and failure. The diagnosis of preeclampsia (International Society for the Study of Hypertension in Pregnancy) is determined by the presence of elevated blood pressure combined with significant proteinuria (≥ 0.3 g/24 hours) after the 20th week of gestation in a previously normotensive, non-proteinuric patient.² One of the cornerstones of antenatal care includes a screening programme directed at the detection of preeclampsia with regular measurements of blood pressure and urinalysis for proteinuria often using urinalysis dipsticks.³ Many methods have been used to shorten the time period to diagnose preeclampsia. Delays may occur in

starting the proper management while laboratory results are awaited or confirmation of diagnosis of preeclampsia may not be possible when patients deliver before the urine sample collection is complete. The laboratory assay methods used also vary widely and the incidence of significant proteinuria has also been shown to vary depending on the assay employed. The gold standard for diagnosis of significant proteinuria is 24-hour urine collection, but 24-hour urine collection is inconvenient for women, costly, and may be inaccurate due to incomplete collection. Also it is also associated with delayed diagnosis and management.⁴

A more rapid test capable of accurately predicting the results of a 24-hour urine would be valuable. An alternative method for quantitative evaluation of proteinuria is the

measurement of spot protein-creatinine ratio (sPCR) in a spot urine sample, which avoids the influence of variations in urinary solute concentration and provides a more convenient and rapid method to assess protein excretion.⁵ A rapid and accurate test may provide efficient inpatient and outpatient monitoring of proteinuria and may shorten the duration of hospitalization. A need therefore exists for a rapid, as well as a valid and accurate test to identify significant urinary proteinuria. This may lead to timely decision making, which is likely to reduce the patients' anxiety, shorten length of hospital stay with its associated cost savings, and target women with true pathology for treatment.⁶

The spot protein to creatinine ratio (sPCR) and albumin to creatinine ratio have been studied extensively outside pregnancy (renal impairment, diabetes, and kidney transplantation); the first ratio has also been studied in hypertensive disorders of pregnancy.⁷ In a study carried out by Obeid N et al⁸ it was seen that 44.0% women have preeclampsia. The sensitivity and specificity of spot urine protein-creatinine ratio in predicting preeclampsia was found to be 86.0% and 76.0% respectively. Bhadarka N et al⁹ have reported the sensitivity and specificity of spot urine protein-creatinine ratio in predicting preeclampsia to be 92.0% and 85.0% respectively. A local study reported the sensitivity and specificity of spot urine protein-creatinine ratio to be 100.0% and 97.14% respectively.¹⁰

Relatively few studies have examined the diagnostic accuracy of albumin to creatinine ratio in pregnancy. Sufficient evidence from studies shows a strong association between spot protein to creatinine ratio and 24 hour protein excretion. The International Society for the Study of Hypertension in Pregnancy has accepted this test as a method for identification of significant proteinuria. However, a consensus has not yet been reached on the most appropriate threshold to be used in clinical practice, specifically in a population with suspected preeclampsia. Therefore we are conducting a study to compare the diagnostic accuracy between 24 hour urinary proteins versus spot protein to creatinine ratio for

diagnosis and determining severity of preeclampsia. There is wide variation in diagnostic accuracy of tests under investigation. We need tests that can ensure rapid diagnosis and treatment thus saving the valuable time of patient and physician.

The objective of this study was to determine the diagnostic accuracy of spot protein creatinine ratio in predicting preeclampsia, taking 24 hours urinary protein as the gold standard. The rationale of this study was to generate local evidence base in this regard. The generated evidence will in turn help to provide guidance for future better management of such patients presenting pre-eclampsia.

Methodology

This descriptive analytical study was conducted at the Department of Obstetrics and Gynecology, Pakistan Institute of Medical Sciences (PIMS), Islamabad, from May 2021 to November 2021. Ethical approval was obtained from the Institutional Review Board (IRB) of Shaheed Zulfiqar Ali Bhutto Medical University (SZABMU) (Reference No.: F.1-1/2015/ERB/SZABMU/727). The study adhered to the ethical principles outlined in the Declaration of Helsinki, as revised in 2013. The anonymity of participants was guaranteed. Informed consent was taken from the patients. Non-probability consecutive sampling technique was employed. Sample size of 156 was calculated by taking 95% confidence level, prevalence of preeclampsia as 44.0% and 10% desired precision for sensitivity and specificity of protein-creatinine ratio in predicting preeclampsia as 86.0% and 76.0% respectively.^{8,11}

The inclusion criteria were pregnant women with suspected preeclampsia, who were aged 20-40 years with singleton pregnancy and a gestational age >20 weeks. Patients having fulminant preeclampsia and those with associated comorbid conditions such as urinary tract infection, gestational diabetes mellitus, chronic hypertension, chronic liver disease and renal disease were excluded.

All the patients were admitted to indoor ward. They underwent thorough clinical evaluation with relevant history, physical examination and necessary investigations. They were investigated

and treated according to the standard protocol within the department for the management of hypertension according to severity of the condition. All women were asked to provide a 24-hour urine collection for the determination of proteinuria. All women were advised to pass urine at 6:00 am and collect all the urine subsequently till 6:00 am the next morning (24-hour period). The adequacy of urine collection was determined by creatinine excretion. Urine sample for protein-creatinine ratio was collected the next morning after the 24-hour collection was over. Urinary protein quantitation was done by Biuret method, and urinary creatinine estimation was done by modified Jaffe's method.

Data were entered and analyzed using SPSS-25. Age, gestational age, protein to creatinine ratio and 24 hours urinary protein levels were presented as mean and SD. Parity (primiparous/multiparous), place of living (rural/urban), h/o previous pre-eclampsia (yes/no) and pre-eclampsia on sPCR and 24 hours urinary protein (present/absent) were presented as frequency and percentage. 2×2 contingency table was used to calculate the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of protein creatinine ratio in predicting pre-eclampsia, taking 24 hours urinary protein as gold standard.

Results

A total of 156 patients were included, all with singleton pregnancies. The age range was 20 to 40 years, with a mean age of 29.68 ± 5.32 years. The majority of patients (n = 83; 53.21%) were between 20 and 30 years of age. The mean gestational age was 26.61 ± 3.15 weeks. The demographic and clinical characteristics of the patients are summarized in Table I.

In 71 sPCR positive patients, 60 (True Positive) had preeclampsia and 11 (False Positive) had no preeclampsia on 24 hours urinary protein. Among, 69 sPCR negative patients, 09 (False Negative) had preeclampsia on 24 hours urinary protein whereas 60 (True Negative) had no preeclampsia on 24 hours urinary protein. Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of sPCR in predicting pre-eclampsia, were 86.96%, 87.36%, 84.51%, 89.41% and 87.18%

respectively. (Table II)

Table I: Demographic and clinical characteristics of the included patients. (n=156)	
Parameters	Number (%)
Mean Age (Years)	29.68 ± 5.32
Mean gestational age (Weeks)	26.61±3.15
Education:	
Primary	124(79.48%)
Middle	25(16.02%)
Higher	7(4.49%)
Social status:	
Poor	130(83.33%)
Middle class	23(14.74%)
Rich	3(1.92%)
Place of living:	
Rural	95(60.89%)
Urban	61(39.10%)
History of previous Preeclampsia:	
Yes	28(17.94%)
No	128(82.05%)
Parity:	
Nulliparous	54(34.61%)
Multiparous	102(65.38%)

Table II: Diagnostic accuracy of spot protein creatinine ratio (sPCR) in predicting pre-eclampsia, taking 24 hours urinary protein as the gold standard. (n=156)			
	Positive result on 24 hours urinary protein	Negative result 24 hours urinary protein	P-value
Positive result on P/C Ratio	60 (TP)*	11 (FP)***	0.0001
Negative result on P/C Ratio	09 (FN)**	76 (TN)****	

TP=True positive **-FP=False positive ***-FN=False negative ****-TN=True negative

Sensitivity: 86.96%

Specificity: 87.36%

Positive Predictive Value (PPV): 84.51%

Negative Predictive Value (NPV): 89.41%

Likelihood ratio for positive test result: 6.88

Likelihood ratio for negative test result: 0.15

Discussion

Our study focused on the diagnosis of preeclampsia. The diagnostic criteria of preeclampsia have remained unchanged for the past several years. These include: a proteinuria reading of ≥30 mg (≥1+on dipstick) in two random urine samples collected at least 4 to 6 hours apart or 24-hour urine protein excretion ≥300 mg/day with

onset at >20 weeks of gestational age, a systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg measured twice. All of these findings should normalize within the 6th postpartum week. The 24-hour urine protein excretion measurement has been the gold standard for quantifying urinary proteins; however it is an inconvenient and time-consuming test. In comparison, the urinary dipstick test may be a quicker and simpler method but its drawbacks are its inconsistency and poor correlation with 24-hour urine protein excretion level, because of its susceptibility to patients' hydration status. In this respect, an alternative method that is as simple and rapid as the dipstick test but with better accuracy in predicting the amount of secreted urinary protein would be valuable.^{1-3, 12, 13}

Our study tested the new modality of sPCR for diagnosis preeclampsia in our pregnant patients. The measurement of a spot urine protein-creatinine (sPCR) ratio has been tested as a substitute for the 24-hour urine protein excretion test for quantifying protein excretion in patients with renal diseases, such as diabetic nephropathy, lupus nephritis, and transplanted kidneys, with good correlation between the two methods. The method relies on calculating the ratio of spot urine protein excretion to creatinine excretion and can normalize the protein excretion to the glomerular filtration rate. Therefore, spot urine PCR is not influenced by variations in hydration status. However, because of the variety of the cutoff values among the past studies, there is no uniform standard so the clinical usefulness of this test still continues to be surrounded by controversies.¹⁴⁻¹⁶

In our study we aimed to determine the diagnostic accuracy of protein creatinine ratio in predicting preeclampsia, taking 24 hours urinary protein as the gold standard. We found the sPCRs to have a sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of 86.96%, 87.36%, 84.51%, 89.41% and 87.18% respectively. In a study performed by Obeid N et al⁸, it was seen that 44.0% women had preeclampsia. The sensitivity and specificity of sPCR in predicting preeclampsia was found to be 86.0% and 76.0% respectively. Bhadarka N et al⁹ have reported the sensitivity and specificity of sPCR in predicting preeclampsia as 92.0% and 85.0% respectively. Basharat et al¹⁰ have reported the

sensitivity and specificity of sPCR to as 100.0% and 97.14% respectively.

Our findings conform to several published studies. For instance, Gai et al¹⁷ proposed that the sPCR could replace the urinary dipstick test, as they found that the highest regression coefficient was between 24-hour urine protein and sPCR ($r=0.72$), and the lowest between sPCR and the urinary dipstick test ($r=0.72$) in patients with renal disease. They also revealed that the urinary dipstick test failed to detect a pathological proteinuria in 31.6% of their study population while sPCR failed to detect it in only 5.4% cases. Meanwhile, in their study with preeclamptic pregnancy, Eigbefoh et al¹⁸ showed that a sPCR had the highest sensitivity (92%), while the urinary dipstick test had a sensitivity of 81%. Their results also showed that the urinary dipstick test had the highest false negative rate (19%), while that of the sPCR was 8%. Furthermore, the specificity for sPCR was 86%, while that for the urinary dipstick test was 47%. Also in their study, the false positive rate was highest with the urinary dipstick test (53%) whereas it was only 14% for sPCR.

A study done by Shahbazian et al¹⁹ identified sPCR of 0.20 g/g as the best threshold to detect urine protein excretion of 300 mg/24h, with sensitivity and a specificity of 91.2% and 87.8% respectively. Wheeler et al²⁰ found strong correlation ($r=0.88$) between the sPCR and 24 h urine protein results, the optimal sPCR based on ROC analysis was 0.21 g/g with sensitivity and specificity of 86.8% and 87.5% respectively. A study by Lamontagne et al²¹ showed a variation in sPCR result during the day. They reported sPCR to be less sensitive in first morning samples. However, Verdonk et al²² compared the sPCR results in three urine sample collected at 8 am 12am and 5 pm and found no difference between the three measurement times regarding the sensitivities and specificities.

As in our study, Sethuram et al²³ also assessed the diagnostic value of sPCR in preeclampsia by correlating it to 24-hour urinary protein. There sensitivity was 83% and specificity was 92%. A similar study was conducted in Larkana. They reported the relationship of sPCR and 24 hour urinary protein excretion to be highly significant and positive in mild to severe proteinuria but not significant in massive proteinuria.²⁴ Cote MA et al²⁵

carried out a systematic review of thirteen studies. They concluded that sPCR was a reasonable rule out test for significant proteinuria of 0.3g/dl or more in pregnancy.

Strengths and limitations of the study: Our study has certain strengths as well as presents some limitations. The major strength of the study was the fact that it tried to document the diagnostic accuracy of spot PRC for preeclampsia among pregnant patients in our hospital. The main limitation was the fact that the study was conducted in a single center. Future well designed long-

term multicenter studies are recommended to improve upon our results.

Conclusion

The diagnostic accuracy of spot urine protein creatinine ratio in predicting preeclampsia was reasonably high. Hence we recommend it as the preliminary screening modality for diagnosing preeclampsia in our pregnant population. It is beneficial on the accounts of its being of economical, simple and fast.

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