Original Article

Diagnostic Accuracy of Spot Protein/Creatinine ratio in Diagnosing Preeclampsia in Pakistani Women Keeping 24 hours Urine Protein as Gold Standard

Sana Hassan[1], Uzma Nayyer[2], Maria Tariq[3], Afnan Rizwan[4], Amarta Imdad Hussain[5], Attiya Irum[6]

[1,5,6]Senior Registrar, [2-4]Assistant Professor

Akbar Niazi Teaching Hospital (ANTH)/IMDC, Islamabad Pakistan

Correspondence: Dr. Maria Tariq
Assistant Professor
Department of Obstetrics and Gynaecology
Islamabad Medical and Dental College
Bhara Kahu, Islamabad
drmaianc300@gmail.com

Abstract

Objective: To assess the diagnostic accuracy of spot protein/creatinine ratio in diagnosing preeclampsia in Pakistani women keeping 24 hours urine protein as gold standard.

Methodology: This cross-sectional validation study was done at Pakistan Ordinance Factory Hospital, Wah Cantt from February 2022 to July 2022. A total of 340 pregnant women with new onset of hypertension, B.P ≥ 140/90 mmHg at two different occasions 6 hours apart were selected. Mid-stream urine sample on the day of admission was send for protein/creatinine ratio and next 24 hours urine sample was collected for 24 hours urinary protein excretion. Selectra-E biuret colorimetric assay was used to measure the total urinary protein and modified Jaffe test was used to measure the urine creatinine.

Results: The women average age was 27.54±3.84 years. The gestational average age was 23.32±2.8 weeks, and the average BMI was 25.38±3.38 Kg/m2. Sensitivity, specificity, PPV, NPV and diagnostic accuracy of spot protein/creatinine ratio in diagnosing preeclampsia were 91.4%, 95.7%, 71.1%, 95.7% and 95.3% respectively.

Conclusion: In conclusion, the ratio of urinary protein/creatinine is a good predictor of proteinuria in preeclampsia and it can replace 24 hours urinary collection as a diagnostic test.

Keywords: Creatinine; Diagnostic equipment; Preeclampsia; Spot protein; Urine protein.

Cite this article as: Hassan S, Nayyer U, Tariq M, Rizwan A, Hussain AI, Irum A. Diagnostic Accuracy of Spot Protein/Creatinine ratio in Diagnosing Preeclampsia in Pakistani Women Keeping 24 hours Urine Protein as Gold Standard. J Soc Obstet Gynaecol Pak. 2023; 13(3):203-206.

Introduction

Early diagnosis of preeclampsia is important as it changes whole management. A 24 hours urine protein count is considered a gold standard to detecting proteinuria in pregnancy. Alternatively, 24 hours urinary protein is urine dipstick, spot protein/creatinine ratio and albumin/creatinine ratio.

Preeclampsia is a multisystem disorder of pregnancy which may complicates fetomaternal outcome. It affects 2-8% of pregnancy.[1] Early diagnosis of preeclampsia is important as it changes whole management. It is defined as a syndrome primarily characterized by onset of hypertension (B.P ≥ 140/90 mmHg) in second half of pregnancy.[2] Most frequently related with proteinuria, other symptoms and signs include epigastric pain, blurring of vision, headache and rapid oedema.[3] Proteinuria is defined as excretion of protein in urine ≥ 300mg/24hours or spot protein/creatinine ratio of ≥ 0.3mg/ml.[4] A 24 hours urine protein count is considered a gold standard to detecting proteinuria in pregnancy.[5] However, it is time consuming, inconvenient, and may be misleading if sample not collected properly.[6] It takes

Authorship Contribution: [1]Concept/research design and did data collection, [2]statistical analysis and manuscript writing, [3]edit of manuscript and project management, [4,5]critical revision of the manuscript for important intellectual content, [6]responsibility and is accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding Source: none
Conflict of Interest: none

Received: May 06, 2023
Accepted: Sept 10, 2023

24 hours to collect the urine sample and few more hours to get the report which leads to prolong hospital stay, less cost effective and most important it delays the diagnosis and management.[7]

Alternatively, 24 hours urine protein is urine dipstick, spot protein/creatinine ratio and albumin/creatinine ratio.[8] Urine dipstick is rapid, easy providing quick results but have low sensitivity and specificity.[9] Recently, the urine protein/creatine ratio is considered important for the calculation of proteinuria in pregnant patients.[5] This compares urinary protein excretion with urinary creatine excretion; thereby regulating protein secretion to glomerular filtration rate. Therefore, it is independent of hydration status of patient.[4] A study conducted in Kolkata University, India suggested that the sensitivity protein/creatine ratio was 91.67%, specificity 80%, with positive predictive value (PPV) 88%, and negative predictive value (NPV) 85.71%. Based on these results, they concluded that random urinary protein excretion predicts 24 hours urinary protein concentration with a high accuracy. It may be a convenient alternative to collecting 24 hours urine to detect significant proteinuria.[10]

A number of studies has been conducted in past few years on the relationship between protein creatinine ratio and 24 hours urine protein, with different results mainly due to different cut-off values used for the protein creatinine ratio and different laboratory methods. Because of this variation, it is difficult to make a fair comparison.[1,5]

The study aim was to determine the sensitivity, specificity, PPV, and NPV of protein/ creatinine ratio, keeping 24 hours urinary protein as gold standard. So, we can substitute it with protein creatinine ratio which is cheap, suitable, less time consuming and early diagnosis that helps in preventing complications of preeclampsia.

Methodology

A cross sectional validation study was done at Pakistan Ordinance Factory Hospital, Wah Cantt from February 2022 to July 2022. After getting approval of ethical review board of the institute and informed written consent from the study participants, total 340 pregnant women (sample size calculation on the bases of sensitivity and specificity and prevalence as follows; 91.7%, 80%, and 8% respectively, and margin of error was 10%),[10] with new onset of hypertension, B.P ≥ 140/90 mmHg at two different occasions 6 hours apart, ages of the women 20-40 years, and gestational age ≥ 20 weeks were selected in this study. The non-probability consecutive sampling was used for enrolled the patients. Patients with following conditions were excluded; chronic hypertension, renal diseases (nephropathies), urinary tract infection, and patient with prolong bed rest.

A specialized proforma had been developed to record the findings of study. All women (n=340) who meet the inclusion criteria of study was admitted. Mid-stream urine sample on the day of admission was send for protein/creatinine ratio and next 24 hours urine sample was collected for 24 hours urine protein excretion. Reports was sent to the hospital laboratory and results were collected. Selectra-E biuret colorimetric assay was used to measure the total urinary protein and modified Jaffe test was used to measure the urine creatinine. The data was entered in the proforma, based on the results all data calculation was done by a senior gynecologist.

Data was analyzed by using SPSS v 25. Frequencies and percentages were calculated for qualitative variables such as test results and parity. Means and standard deviations were calculated for age, gestational age, and BMI. Accuracy is measured in terms of sensitivity, specificity, PPV and NPV. The likelihood ratio was also computed, and AUC by ROC were drawn. Effect modifier like age, parity, and BMI were controlled through stratification and sensitivity, specificity, PPV, NPV, and accuracy were measured.

Results

Total 340 pregnant women were enrolled. The average age of the women was 27.54±3.84 years. The average gestational age was 23.32±2.8 weeks, and average BMI was 25.38±3.38 Kg/m^2. Out of 340, 92 (27.06%) women had primiparous, and 248 (72.89%) multiparous.

Preeclampsia was observed in 10.3% women confirmed by 24 hours urinary protein. While, according to spot protein/creatinine ratio identified 13.2% preeclamptic cases (Table I). Area under the curve by ROC was 0.97 which is significantly high cutoff diagonal line (0.50) (Figure 1).

Age, and parity were stratified and observed that was above 90%. In age group of ≤ 30 years, the sensitivity, specificity, PPV, NPV and accuracy of spot protein/creatinine ratio in diagnosing preeclampsia were 90.9%, 96.1%, 75.0%, 98.8%, 95.8%,

respectively and likelihood ratio 23.18. In age group of ≥ 30 years, the sensitivity, specificity, PPV, NPV and accuracy of spot protein/creatinine ratio in diagnosing preeclampsia were 100%, 94.0%, 40.0%, 100%, 94.2%, respectively and likelihood ratio 16.67.

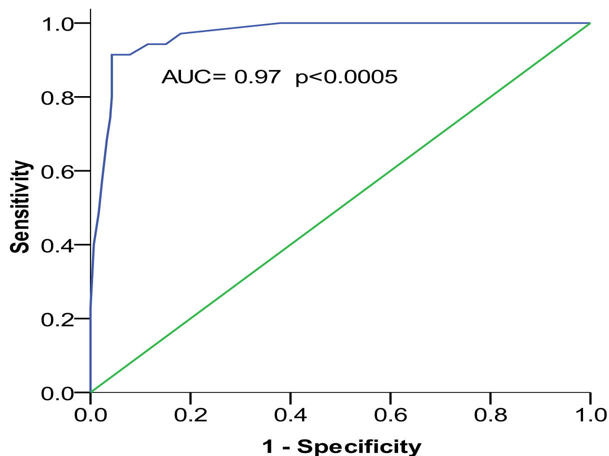

Figure 1. Receiver operating curve (ROC), spot protein/creatinine ratio in diagnosing preeclampsia, (n=340)

The parity status of primiparous was observed as follows; the sensitivity, specificity, PPV, NPV and accuracy of spot protein/creatinine ratio in diagnosing preeclampsia were 85.7%, 96.2%, 80%, 97.4%, 94.5%, respectively and likelihood ratio 22.29. Whereas, the parity status of multiparous was observed as follows; the sensitivity, specificity, PPV, NPV and accuracy of spot protein/creatinine ratio in diagnosing preeclampsia were 95.2%, 95.6%, 66.7%, 99.5%, 95.6%, respectively and likelihood ratio 21.62.

Table I: Spot protein/creatinine ratio in diagnosing preeclampsia. (n=340)

Spot protein/creatinine ratio	24 hours urine protein		Total
	Positive ≥ 300mg	Negative ≤ 300mg	
Positive ≥ 0.30	32	13	45 (13.2%)
Negative ≤ 0.30	3	292	295 (86.8%)
Total	35 (10.3%)	305 (89.7%)	340
Sensitivity	91.4%		
Specificity	95.7%		
PPV	71.1%		
NPV	95.7%		
Accuracy	95.3%		
Likelihood ratio +	21.45		

Discussion

The current study aim was to assess the diagnostic accuracy of spot protein/creatinine ratio in diagnosing preeclampsia in Pakistani women keeping 24 hours urine protein as gold standard. In this study, preeclampsia was observed in 10.3% women confirmed by 24 hours urinary protein while according to spot protein/creatinine ratio identified 13.2% preeclamptic cases. Sensitivity, specificity, PPV, NPV and accuracy of spot protein/creatinine ratio in diagnosing preeclampsia in Pakistani women keeping 24 hours urine protein as gold standard was 91.4%, 95.7%, 71.1%, 95.7% and 95.3% respectively. Area under the curve by ROC was 0.97 which is significantly high cutoff diagonal line (0.50) showing high accuracy. Our results are supported by other studies. A meta-analysis study found maternal uPCR presented diagnostic value for suspected proteinuria in preeclampsia.[11] In our study, the ROC curve was 0.97, which is comparable to the results of a meta-analysis, pooled ROC curve was 0.90, and combined sensitivity and specificity were 91% and 86.3%, respectively.[12] Sethuram et al evaluated the diagnostic value of the correlation of point protein for creatine ratio with 24 hours urinary protein in preeclampsia. Compared to our study, the sensitivity was 83% and the specificity was 92%.[13] The NPV of urinary protein/creatine ratio is as high as 95.7% and did not change significantly with the protein-creatine ratio cutoff for diagnosis of proteinuria.

Maternal death due to eclampsia is 2nd common cause in Pakistan.[14] A hospital-based study also found hypertensive disorders as the etiology of maternal mortality.[15] The proteinuria diagnosis in the occurrence of ≥ 300 mg protein in 24 hours urinary sample is a gold standard.[16] While, these tests are difficult, and time-consuming, have costs, can delays in diagnosis and interventions due to change in time, and inappropriate findings from imperfect sample collections or different views. There is a close correlation between the ratio of protein to creatinine in urinary samples and 24 hours protein analyzed by 24 hours urine collection.[17]

The current study gives the accuracy of uPCR and its association with outcomes of pregnancy in the indigenous population of Pakistan. The technique of determining proteinuria by protein/creatinine ratio helps diagnose faster and more reliably, and gives better fetal results in the early stages of treatment.

Conclusion

In conclusion, the ratio of urinary protein/creatinine is a good predictor of proteinuria in preeclampsia and it can replace 24 hours urinary collection as a diagnostic test.

The ratio of creatine-to-protein can be reliable, fast, and accurate for proteinuria, so the short time for the diagnosis of preeclampsia will be valuable in reducing hospital costs and the patient's discomfort for the purpose of treatment. Early diagnosis ensures a good fetal outcome.

References

1. Mahesh S, Borgohain D. Spot urinary albumin-to-creatinine ratio: a novel marker for detecting fetomaternal outcomes and complications in preeclamptic women. J Obstet Gynaecol India. 2020;70(2):30-35. https://doi.org/10.1007/s13224-019-01264-w
2. Makhmudova SE, Ataeva FN. Evolutionary views on hypertensive disorders in pregnancy (literature review). In Advanced Science. 2019:183-187.
3. Narkhede AM, Karnad DR. Preeclampsia and Related Problems. Indian J Crit Care Med. 2021;25(Suppl 3):S261-S266. https://doi.org/10.5005/jp-journals-10071-24032
4. Wilkerson RG, Ogunbodede AC. Hypertensive disorders of pregnancy. Emerg Med Clin. 2019;37(2):301-316. https://doi.org/10.1016/j.emc.2019.01.008
5. Stefanska K, Zielinski M, Zamkowska D, Adamski P, Jassem-Bobowicz J, Piekarska K, et al. Comparisons of dipstick test, urine protein-to-creatine ratio, and total protein measurement for the diagnosis of preeclampsia. Int J Environ Res Public Health. 2020;17(12):4195. https://doi.org/10.3390/ijerph17124195
6. Shah S, Sulthana P. A Comparative Study of Urine Dipstick and Urine Protein Creatinine Ratio with 24 Hour Urinary Protein in Estimation of Significant Proteinuria in Pre-Eclampsia. IOSR J Dent Med Sci. 2019;18(7):21-29.
7. Demirci O, Kumru P, Arinkan A, Ardic C, Arisoy R, Tozkir E, et al. Spot protein/creatinine ratio in preeclampsia as an alternative for 24-hour urine protein. Balkan Med J. 2015;32(1):51-55. https://doi.org/10.5152/balkanmedj.2015.15447
8. Rao S, Somalwar S, Bhalerao A, Raman V, Rao Jr S, Raman Jr V. Accuracy of Spot Urine Albumin Creatinine Ratio with Respect to 24-Hour Urine Albumin for the Detection of Proteinuria in Antenatal Women with Preeclampsia: A Descriptive Study. Cureus. 2023;15(6):e39961. https://doi.org/10.7759/cureus.39961
9. Davenport M, Mach KE, Shortliffe LM, Banaei N, Wang TH, Liao JC. New and developing diagnostic technologies for urinary tract infections. Nat Rev Urol. 2017;14(5):296-310. https://doi.org/10.1038/nrurol.2017.20
10. Hossain S, Ghosh A, Chatterjee A, Sarkar G, Mondal SS. To evaluate the diagnostic value of protein: creatinine ratio in a single voided urine sample for quantitation of proteinuria compared to those of a 24-hour urine sample in patients with preeclampsia. J Coll Med Sci Nepal. 2013;9(2):45-53. https://doi.org/10.3126/jcmsn.v9i2.9687
11. Morris RK, Riley RD, Doug M, Deeks JJ, Kilby MD. Diagnostic accuracy of spot urinary protein and albumin to creatinine ratios for detection of significant proteinuria or adverse pregnancy outcome in patients with suspected pre-eclampsia: systematic review and meta-analysis. BMJ. 2012;345(7):e4342. https://doi.org/10.1136/bmj.e4342
12. Sanchez-Ramos L, Gillen G, Zamora J, Stenyakina A, Kaunitz AM. The protein-to-creatinine ratio for the prediction of significant proteinuria in patients at risk for preeclampsia: a meta-analysis. Ann Clin Lab Sci. 2013;43(2):211-220.
13. Sethuram R, Kiran TU, Weerakkody AA. Is the urine spot protein/creatinine ratio a valid diagnostic test for pre-eclampsia?. J Obstet Gynaecol. 2011;31(2):128-130. https://doi.org/10.3109/01443615.2010.538771
14. Akhtar R, Shams G, Afzal I, Ajmal B. Maternal mortality, a major loss-trends and causes. KJMS: Khyber J Med Sci. 2021;14(3):180-184.
15. Shah N, Hossain N, Shoaib R, Hussain A, Gillani R, Khan NH. Socio-demographic characteristics and the three delays of maternal mortality. J Coll Physicians Surg Pak. 2009;19(2):95-98.
16. Tranquilli A, Dekker G, Magee L, Roberts J, Sibai BM, Steyn W, et al. The classification, diagnosis and management of the hypertensive disorders of pregnancy: a revised statement from the ISSHP. Pregnancy Hypertens. 2014;4(2):97-104. https://doi.org/10.1016/j.preghy.2014.02.001
17. Teeuw HM, Amoakoh HB, Ellis CA, Lindsley K, Browne JL. Diagnostic accuracy of urine dipstick tests for proteinuria in pregnant women suspected of preeclampsia: A systematic review and meta-analysis. Pregnancy Hypertens. 2022;27(3):123-130. https://doi.org/10.1016/j.preghy.2021.12.015