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DIAGNOSTIC ACCURACY OF SPOT URINE PROTEIN TO CREATININE RATIO FOR ESTIMATION OF SIGNIFICANT PROTEINURIA IN PATIENTS OF PREECLAMPSIA

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ABSTRACT

OBJECTIVE: To determine diagnostic accuracy of spot urine protein to creatinine ratio (PCR) for estimation of significant proteinuria in patients of preeclampsia based on 24-hour urine protein.

METHODS: This cross-sectional validation study was conducted at Gynae B unit, Lady Reading Hospital, Peshawar from July 2014 to December 2014. Out of 253 patients, 222 women were finally enrolled as per inclusion and exclusion criteria by using non-probability convenient sampling technique. After taking proper history and calculating period of gestation, blood pressure was measured using standard sphygmomanometer while urinary protein by urine dipsticks. Following standard protocol, urine was collected for 24 hours followed by spot midstream urine. Samples were analyzed for urine protein and creatinine. 24 hours urinary protein level ≥300 mg/day and spot urine PCR was ≥3 mg/mmol was considered significant proteinuria. SPSS v 16.0 was used a statistical instrument.

RESULTS: Out of 222 patients with preeclampsia, 24-hours urinary protein level estimation was ≥300 mg/day in 179 (80.6%) cases and <300 mg/day in 43 (19.4%) cases. Spot urine PCR was ≥3 mg/mmol in 175 (78.8%) cases and <3 mg/mmol in 47 (21.2%) cases. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy of spot urine PCR against 24-hours urinary protein level estimation was 95.5%, 90.6%, 97.7% 82.9% and 94.5% respectively.

CONCLUSION: In our study, spot urinary protein/ creatinine ratio shows a high sensitivity, specificity, PPV, and NPV (at a cut off value >0.3 mg/mmol). This test can be regarded as a reliable investigation among pre-eclamptic patients.

KEY WORDS: Diagnostic accuracy (Non-MeSH); Urine proteins (Non-MeSH); Creatinine (MeSH); Proteinuria (MeSH); Pre-Eclampsia (MeSH); Sensitivity and Specificity (MeSH); Positive Predictive Value (MeSH); Negative Predictive Value (MeSH).

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INTRODUCTION

Hypertensive disorders in pregnancy are liable for substantial maternal and perinatal morbidities and is the second foremost cause following hemorrhage in maternal mortality. It accounts for 15% of all direct maternal deaths in UK, 24% in India, and 30% in Pakistan.[1,2] Detection of proteinuria is integral part of investigations in hypertensive diseases of pregnancy and used to differentiate preeclampsia from other types i.e. non-proteinuric gestational hypertension and chronic hypertension.[1] The criterion test for diagnosis of preeclampsia is 24 hour urinary protein in which a value ≥300mg/day predicts significant proteinuria.[3,4] However the urine collection in pregnancy can be inadequate due to increase in ureteral dead spaces, the inconvenient tests, and low reliability in correctly identifying proper method of urine collection, which is cumbersome or time consuming both for patient and laboratory, and hence, delays the diagnosis of disease leading to extended hospital stay of patients.[3,5,6] A more rapid and quicker test is urine dipstick analysis, +1 proteinuria on dipstick match up to 300mg/24 hours urinary proteins excretion. But the test is poorly correlated with 24 hours urine proteins and has high false negative and positive rates of 66% and 26% respectively.[7]

A substitute method for quantification of proteinuria is the determining ratio of spot urine protein to creatinine (spot test), which is simple, rapid, less expensive, and not influenced by hydration status of patient.[3,5] The prime cut off value for significant proteinuria is > 0.19mg/mg or 30mg/mmol.[4,8] The sensitivity and specificity of the test as determined by Price et al. is 69% and 41% respectively[9] whereas in some studies its sensitivity and specificity was found to be as high as 80% and 68% respectively.[4] The usefulness of this test is well established in non-pregnant population.[10] Several international organizations have accepted this test for quantification of proteinuria in pregnancy i.e. International Society for the Study of hypertension, Society of Obstetric Medicine of Australia and New Zealand and the Society of

TABLE I: CROSS TABULATION FOR SPOT URINE PROTEIN- CREATININE RATIO WITH 24 HOURS URINARY PROTEIN LEVEL

Variable		24 Hours Urinary Protein Level ≥ 300 mg/day		Total
		Yes	No	
Spot Urine Protein-Creatinine Ratio ≥ 3 mg/mmol	Yes	171 (98%)	4 (2%)	175 (78.8%)
	No	8 (16%)	39 (84%)	47 (21.2%)
	Total	179 (80.6%)	43 (19.4%)	222 (100%)

TABLE II: DIAGNOSTIC ACCURACY OF SPOT URINE PROTEIN TO CREATININE RATIO

Statistical Analysis		%age
Sensitivity	TP/TP+FN	95.5%
Specificity	TN/TN+FP	90.6%
Positive predictive value	TP/TP+FP	97.7%
Negative predictive value	TN/TN+FN	82.9%
Diagnostic accuracy	TP+TN/TP+TN+FP+FN	94.5%

TP: True positive; TN: True Negative; FP: False positive; FN: False Negative

Obstetricians and Gynecologists of Canada.[2]

Due to scarcity of local data on this topic and increasing load of preeclampsia patients in our hospital, the goal of our study was to determine diagnostic accuracy of the ratio of spot urine protein to creatinine ratio (PCR) used to predict significant preteinuria in patients of preeclampsia as a substitute to the 24 hour urine protein. The 24 hour urine protein is more time consuming, delays the diagnosis of preeclampsia, and hence putting the mother and fetus at risk. Thus, this quicker and convenient test can relieve patient from anxiety in a manageable health care cost which otherwise suffer due to prolonged hospital stay for the 24 hours test.

METHODS

This cross-sectional validation study was conducted at Unit B of Gynecology Department, Lady Reading Hospital, Peshawar from July 2014 to December 2014. Out of the total of 253 patients, 222 women with singleton pregnancy and after 20 weeks period of gestation fulfilling the operational definition of preeclampsia were included in the study while 31 patients with medical conditions such as multiple pregnancies, active urinary tract infections, gestational or known diabetics, chronic hypertension, patients with known kidney diseases i.e. protein loosing nephropathies, bed rest > 24 hours, orthostatic proteinuria, and mothers who delivered their babies during urine-collection day were excluded from the study. Detailed history was taken from each subject. Period of gestation was calculated either by dates or by 1st trimester scan. Blood pressure of the subjects was checked with standard sphygmomanometer and urine protein using urine dipsticks. This study was approved by the Hospital Ethics Committee and informed consent was obtained from each patient included in the study. After discarding the first voided urine, 24 hours urine collection was started from morning 8:00 AM till next morning 8:00 AM in a graduated jar. Spot midstream urine was obtained after the completion of 24 hours urine collection and samples were codified. All specimens were carried to laboratory of LRH, Peshawar within 1 hour to avoid potential errors of prolonged stay. Tests were carried out by a consultant pathologist. In spot specimen random urine protein and 24 hours urine protein were measured by colorimetric method using Microlab 300 machine (ELITech Group France). Urine creatinine was determined by creatinine Jaffe method using Hitachi 902 auto analyzer machine (Japan). The data was recorded in specially designed proforma. All the information extracted was then analysed through Statistical Package for Social Sciences (SPSS) Version 16.

RESULTS

In this study, 62 (28%) patients were of the age less than 20 years, 115 (52%) patients were in age range 21-30 years and 45 (20%) patients were in age range 31-40 years. Mean age was 26.83±9.32. The 24 hours urinary protein level was analyzed among 222 patients. In 179/222 (80.6%) patients, urinary protein level was ≥ 300 mg/dl while in 43/222 (19.4%) patients the level of urinary protein was <300 mg/dl. Mean urinary protein level was 360±2.71 mg/dl. Spot urine protein-creatinine ratio was also analyzed among 222 patients and it was found that 175/222 (78.8%) patients had spot urine PCR ≥ 3 mg/mmol while 47/222 (21.2%) patients had spot urine PCR < 3 mg/mmol.

Diagnostic accuracy for spot urine PCR taking 24 hours urinary protein level was analyzed and we found that sensitivity was 95.5% and specificity 90.6% (Table II).

DISCUSSION

Pre-eclampsia is a noteworthy contributor to maternal mortality. Risk typically increases when the patient present with increased blood pressure. Besides the blood pressure criteria to diagnose pre-eclampsia, one another option is to explore the existence of significant proteinuria. The gold standard for proteinuria, is a 24-hour urinary protein excretion, which is unwieldy both for the patients and staff handling the urine collection. The same procedure is prone to errors owing to erroneous timing and/or incompleteness. Preeclampsia is diagnosed by the existence of high blood pressure and significant proteinuria (300 mg per 24 h) after the 20th week of gestation.[10] The 24-hrs urine collection is the bench mark for measuring proteinuria.[11] However unfortunately, 24-h urine collection requires a whole day, and thus, not much useful in making clinical assessments upon first evaluation. This can delay the diagnosis and hence treatment.[12] A quick screening test to envisage 24-hrs proteinuria in blend

TABLE III: COMPARISION OF SPOT URINE PROTEIN TO CREATININE RATIO DIAGNOSTIC ACCURACY IN DIFFERENT RESEARCHES

Researcher	Sensitivity	Specificity	PPV	NPV
Shahbazian N, et al[14]	91.2%	87.8%	94.4%	96.8%
Leaños-Miranda A, et al.[15]	98.2%	98.8%	97.2%	99.2%
Cade TJ, et al.[11]	66%	95%	-	-
Eslamina L, et al.[6]	87.9%	92.6%	90.6%	89.3%
Durnwald, et al[16]	72.6%	73%	45.2%	89.7%
Sharma A, et al[17]	99.1%	100%	-	-

with other presenting signs & symptoms, can aid a clinician to conclude proper surveillance during the initial 24-hrs period.[13] Diagnostic accuracy of spot urine PCR taking 24 hours urinary protein level as a gold standard was analyzed as the sensitivity was 95%, specificity 90%, PPV was 98%, NPV was 83% in this study.

Similar results were found by different researchers who studied spot urine PCR vs. 24 hours urinary protein excretion in women with pre-eclampsia and reported high values of sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) as given in Table III.

Of all these researchers, the study by Cade TJ, et al.[11] reported a lower values of sensitivity of urinary PCR for detection of proteinuria (at a value of > 0.3) that is 66% and a specificity of 95% and rated the test as unreliable. Similarly Durnwald, et al.[17] did not show a high sensitivity or specificity; they found that test had a lower sensitivity of 72.6% and lower specificity of 73%. The authors also documented a low PPV and NPV of 45.2% and 89.7% respectively. However, the cut off value in their study was > 0.3, which was a bit higher than this study. Several cut-off and different units have been reported for PCR value in different reported studies. Dwyer BK, et al.[12] had reported optimal cut–off points as 0.15-0.5mg/mg and observed a high frequency of patients who were positive for proteinuria.

CONCLUSION

This study concluded that spot urinary protein/ creatinine ratio shows a high sensitivity, specificity, PPV, and NPV (at a cut off value >0.3). This test can be regarded as a reliable investigation among pre-eclamptic patients. The spot urine protein creatinine ratio can provide excellent intuition between patients with and without significant proteinuria. This test can be of great help for making quick clinical decision instead of waiting for 24-hour urine collection.

REFERENCES

1. Shaikh SA, Shaikh S Shaikh GS. Optimal diagnostic value of random urine protein to creatinine ratio over 24 hour urine excretion in women with preeclampsia at Chandka Medical College Hospital Larkana. Med Channel 2010;16(3) 413-16.
2. Sultan N. Pregnancy in Pakistan. The forgotten millennium development goal? A Global Village 2011;(3):51-3. Available from URL: https://aglobalvillage.org/journal/issue3/in_the_field/pregnancy-in-pakistan/
3. Huang Q, Gao Y, Yu Y, Wang W, Wang S, Zhong M. Urinary Spot Albumin: Creatinine Ratio for Documenting Proteinuria in Women With Preeclampsia. Rev Obstet Gynecol 2012;5(1):9-15.
4. Rizk D, Agarwal MM, Pathan JY, Obineche EN. Predicting proteinuria in hypertensive pregnancies with urinary protein-creatinine or calcium-creatinine ratio. J Perinatol 2007;27(5):272–7. DOI: 10.1038/sj.jp.7211689.
5. Park JH, Chung D, Cho HY, Kim YH, Son GH, Park YW, et al. Random urine protein/creatinine ratio readily predicts proteinuria in preeclampsia. Obstet Gynecol Sci 2013;56(1):8-14.
6. Eslamian L, Behnam F, Tehrani ZF, Jamal A, Maroosi V. Random Urine Protein Creatinine Ratio as a Pre admission Test in Hypertensive Pregnancies with Urinary Protein Creatinine Ratio. Acta Med Iran 2011;49(2):81-4.
7. Sheikh F, Venyo A. Proteinuria in Pregnancy: A Review of the Literature. Webmd Central Obstet Gynaecol 2012;3(11): WMC003814. DOI: 10.9754/journal.wmc.2012.003814.
8. Waugh JJS, Smith MC. Hypertensive disorders. In: Edmonds K. Dewhurst textbook of obstetrics and gynaecology. 8th Edition: Wiley-Blackwell;2012.p.101-9.
9. Price CP, Newall RG, Boyd JC. Use of Protein: Creatinine Ratio Measurements on Random Urine Samples for Prediction of Significant Proteinuria: A Systematic Review. Clin Chem 2005;51(9):1577-86. DOI: 10.1373/clinchem.2005.049742.
10. Aggarwal N, Suri V, Soni S, Chopra V, Kohli HS. A prospective comparison of spot urine protein-Creatinine ratio versus 24-hour urinary protein excretion in women with preeclampsia. Medscape J Med 2002; 10(4):98.
11. Cade TJ, Gilbert SA, Polyakov A, Hotchin A. The accuracy of spot urinary protein-to-creatinine ratio in confirming proteinuria in pre-eclampsia. Aust N Z J Obstet Gynaecol 2012;52(2):179-82. DOI: 10.1111/j.1479-828X.2011.01409.x.
12. Dwyer BK, Gorman M, Carroll IR, Druzin M. Urinalysis vs. urine protein–creatinine ratio to predict significant proteinuria in pregnancy. J Perinatol 2008;28(7):461-7. DOI: 10.1038/jp.2008.4.
13. Roudsari FV, Ayati S, Ayatollahi H, Shakeri MT. Protein/creatinine ratio on random urine samples for prediction of proteinuria in preeclampsia. Hypertens Pregnancy 2012;31(2):240-42.DOI: 10.3109/10641955.2010.507838.
14. Shahbazian N, Hosseini AF. A comparison of spot urine protein-creatinine ratio with 24 hour urine

protein excretion in women with pre-clampsia. Iranian J Kidney Dis 2008;2(3):127-31.

15. Leanos-Miranda A, Marquez-Acosta J, Romero-Arauz F, Cardenas-Mondragon GM, Rivera-Leanos R, Isordia-Salas I, et al. Protein: creatinine ratio in random urine samples is a reliable marker of increased 24-hour protein excretion in hospitalized women with hypertensive disorders of pregnancy. Clin Chem 2007; 53(9):1623–28. DOI: 10.1373/clinchem.2007.089334.
16. Durnwald C, Mercer B. A prospective comparison of total protein/creatinine ratio versus 24-hour urine protein in women with suspected preeclampsia. Am J Obstet Gynecol 2003;189(3):848-52. DOI: 10.1067/s0002-9378(03)00849-4.
17. Sharma A, Kiran P, Ajaj B. Spot urine protein/creatinine ratio—A quick and accurate method for diagnosis of preeclampsia. Open J Gynaecol Obstet 2013;3(8):609-12

AUTHORS' CONTRIBUTIONS

Following authors have made substantial contributions to the manuscript as under:

SS: Conception and study design, drafting the manuscript, final approval of the version to be published

RA & BR: Analysis and interpretation of data, critical review, final approval of the version to be published

SA: Acquisition, analysis and interpretation of data, drafting the manuscript, final approval of the version to be published

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity ofany part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST

Authors declared no conflict of interest

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