CORRELATION OF SPOT URINE ALBUMIN AND 12-HOUR URINE PROTEIN WITH 24-HOUR URINE PROTEIN IN PRE-ECLAMPSIA

S. Vinayachandran[1], Darsana K[2]

[1]Professor, Department of Obstetrics and Gynaecology, Institute of Maternal and Child Health, Government Medical College, Kozhikode, Kerala.
[2]Senior Resident, Department of Obstetrics and Gynaecology, Institute of Maternal and Child Health, Government Medical College, Kozhikode, Kerala.

ABSTRACT

BACKGROUND

Pre-eclampsia is defined as the development of new-onset hypertension in the second half of pregnancy often accompanied by new-onset proteinuria with other signs and symptoms. Proteinuria is defined by the excretion of 300 mg or more of protein in a 24-hour urine collection. To avoid time consumed in collection of 24-hour urine specimens, efforts have been made to develop faster methods to determine concentration of urine protein. Preliminary studies have suggested that 12-hour urine protein collection maybe adequate for evaluation of pre-eclampsia with advantage of early diagnosis and treatment of pre-eclampsia as well as potential for early hospital discharge and increased compliance with specimen collection.

The aim of the study is to evaluate and correlate spot urine albumin and 12-hour urine protein with 24-hour urine protein in pre-eclampsia.

MATERIALS AND METHODS

A diagnostic evaluation study- a 24-hour urine protein, 12-hour urine protein and spot urine albumin results are analysed. Correlation of 12-hour urine protein and spot urine albumin with 24-hour urine protein is analysed using SPSS software. The strength of correlation was measured by Pearson's correlation coefficient (r). Student's t-test and Chi-square tests were used to compare patients with and without 24-hour urine protein ≥300 mg. Probability value of <0.05 was considered statistically significant.

RESULTS

Of the 300 patients in the study, 111 women had 24-hour urine protein ≥300 mg, 12-hour urine protein was ≥165 mg in 115 patients, 12-hour urine protein estimation correlate with 24-hour urine protein with r value 0.983 and p value 0.000. Sensitivity 94.5%, specificity 94.7%, positive predictive value 91.3% and negative predictive value 96.7%. Spot urine albumin was 1+ or above in 67 patients and was nil or trace in 233 patients. Spot urine albumin correlate with 24-hour urine protein with r value 589 and p value 0.000, sensitivity 45.94%, specificity 91.5%, positive predictive value 76.11% and negative predictive value 74.2%.

CONCLUSION

The high correlation of 12-hour urine protein >165 mg with 24-hour urine protein ≥300 mg suggest that this test has role in the evaluation of women with suspected pre-eclampsia and could be substituted for 24-hour urine protein as a simple, faster and cheaper method.

KEYWORDS

12-Hour Urine Protein, 24-Hour Urine Protein, Urine Spot Albumin, Pre-eclampsia.

HOW TO CITE THIS ARTICLE: Vinayachandran S, Darsana K. Correlation of spot urine albumin and 12-hour urine protein with 24-hour urine protein in pre-eclampsia. J. Evid. Based Med. Healthc. 2017; 4(91), 5486-5490. DOI: 10.18410/jebmh/2017/1096

BACKGROUND

Hypertensive disorders complicate 5-10% of all pregnancies. Pre-eclampsia is identified in 3.9% cases. It remains a leading cause of maternal and neonatal morbidity and mortality worldwide.[1]

Pre-eclampsia is best described as a pregnancy-specific syndrome that can affect virtually every organ system.[2] It chiefly includes the development of new-onset hypertension in the second half of pregnancy. Although, often accompanied by new-onset proteinuria, pre-eclampsia can be associated with many other signs and symptoms including visual disturbances, headaches, epigastric pain and rapid development of oedema.[2]

Proteinuria is defined by the excretion of 300 mg or more of protein in a 24-hour urine collection. Alternatively,

Financial or Other, Competing Interest: None.
Submission 18-10-2017, Peer Review 25-10-2017,
Acceptance 18-11-2017, Published 23-11-2017.
Corresponding Author:
Dr. Darsana K,
'Sudarsana', Keloth,
Payyannur, Kannur – 670307.
E-mail: dkannoth@gmail.com
DOI: 10.18410/jebmh/2017/1096

a protein/creatinine ratio of at least 0.3 or a dipstick reading of 1+ also suggests proteinuria.[1] In the absence of proteinuria that meets or exceeds the diagnostic threshold, any of the following can establish the diagnosis- new-onset thrombocytopenia, impaired liver function, renal insufficiency, pulmonary oedema or visual or cerebral disturbances.[1]

To avoid the time consumed in collection of 24-hour urine specimens, efforts have been made to develop faster methods to determine concentration of urine protein. One of these methods is the dipstick that has a good, although not perfect correlation with protein concentration in urine. A 1+ dipstick has a 92% positive predictive value to predict >300 mg of protein. However, a negative to trace dipstick result does not rule out proteinuria and up to 66% of these patients will have ≥300 mg of protein in a 24-hour urine collection. The correlation of dipstick with 24-hour of protein was studied by Meyer et al (1994).[3]

The 24-hour period required for collection of urine may result in a delay in diagnosis and treatment or possibility of prolonged hospital stay. Shortening the period for diagnosis of pre-eclampsia would be valuable for management purposes as well as decreasing hospital cost and patient inconvenience. More rapid methods of identifying proteinuria such as protein-creatinine ratios and dipstick have not been shown to correlate with disease severity as determined by 24-hour urine collections.[4]

Preliminary studies have suggested that 12-hour urine protein collection (as opposed to 24-hour urine protein) maybe adequate for evaluation of pre-eclampsia with advantage of early diagnosis and treatment of pre-eclampsia as well as potential for early hospital discharge and increased compliance with specimen collection.[4]

Adelberg et al in a prospective observational study of 65 patients used Receiver Operating Characteristic (ROC) to determine the optimal cut off for proteinuria (>165 mg) in the 12-hour urine sample to diagnose pre-eclampsia accurately (78% sensitivity, 100% specificity, 100% positive predictive value and 71% negative predictive value, p value <0.001).[5]

Christina Tun et al in a prospective observational study of 90 women admitted with suspected pre-eclampsia found out that 12-hour urine protein >165 mg correlated significantly with 24-hour urine protein ≥300 mg (r=0.99; p value <0.001) (sensitivity 96%, 100% specificity, 100% positive predictive value and 98% negative predictive value.).[4]

MATERIALS AND METHODS

In this diagnostic evaluation study conducted at Department of Obstetrics and Gynaecology, Government Medical College, Kozhikode, 300 pregnant patients aged 18-40 yrs. who were admitted with gestational hypertension or chronic hypertension were included in the study. Known pre-pregnancy renal disease, upper urinary tract infection with positive urine culture and fever and those who did not give informed consent were excluded.

Methodology- Pregnant women coming under inclusion criteria is selected for the study. An informed written consent is taken. Patients' details are recorded as per pro forma. Spot urine albumin 12-hour and 24-hour urine of each patient is collected after admission irrespective of the time of the day. A 24-hour urine is collected in 2 consecutive 12-hour urine collections. The container were marked with patient's name, IP number and collection time and date. Container were sent to laboratory in IMCH where spot urine albumin is estimated by dipstick method and protein from 12-hour and 24-hour urine sample is estimated by EM 200 automated analyser using pyrogallol red reagent.

Total protein for 12-hour is calculated by multiplying 12-hour urine volume in decilitre by concentration of protein in test sample (mg/dL). Value of ≥165 mg in 12-hour urine is taken as significant.

Total protein for 24-hour is calculated by multiplying 24-hour urine volume in decilitre by concentration of protein in test sample (mg/dL). Total protein of 24-hour is calculated by combining both 12-hour urine specimens. Value of ≥300 mg in 24-hour urine is taken as significant.

Data entry was done in Microsoft excel programme. Correlation of 12-hour urine protein and spot albumin with 24-hour urine protein analysed using SPSS software version 16.0 for windows. Qualitative data was expressed as frequency and percentages and quantitative data as mean or median with standard deviation. The strength of correlation was measured by Pearson's correlation coefficient (r). Student's t-test and Chi-square tests were used to compare characteristics of women with and without 24-hour urine protein >/=300 mg. A probability value of <0.05 was considered statistically significant.

RESULTS

Mean age of the patients in the study was 26.49 ± 5.075 years. Majority among them were primigravidas constituting 52% and multigravidas 48%. Among multigravidas, 17.3% had previous history of pre-eclampsia. Family history of pre-eclampsia was present in 3% of patients.

The mean gestational age was 36.97 ± 2.407 weeks with range of 26 weeks - 40 weeks. The mean blood pressure of the patients was 149.87 ± 12.62 mmHg systolic and 98.11 ± 7.39 mmHg diastolic.

Most common indication for admission was elevated blood pressure (72.66% cases). Other indications included foetal growth restriction, symptoms like headache, blurring of vision, oedema and abdominal pain and laboratory abnormalities.

Correlation of 12-hour urine protein and spot urine albumin with 24-hour urine protein.

Of the 300 patients in the study group, 111 (37%) women had 24-hour urine protein ≥300 mg and 12-hour urine protein was >165 mg in 115 (38.33%) of patients. Among the 111 patients with pre-eclampsia diagnosed with 24-hour urine protein ≥300 mg, 107 patients showed 12-hour urine protein ≥165 mg. A 12-hour urine protein was falsely positive in 8 patients. Sensitivity of 12-hour urine protein for the diagnosis of pre-eclampsia is 96.39% with

positive predictive value of 93.04%. Specificity is 95.76% with negative predictive value of 97.83%. A 12-hour urine protein values positively correlated with 24-hour urine protein, which is statistically significant with r value 0.983 and p value 0.000.

67 patients had spot urine albumin 1+ or above and was nil/trace in 233 patients. Of the 233 patients with spot urine albumin nil/trace, 173 (74.24%) had no significant proteinuria (<300 mg/24 hours), while 60 patients (25.75%) had proteinuria ≥300 mg/24 hours. 29 patients in the study had spot urine albumin 1+ of which only 15 (51.72%) had significant proteinuria (≥300 mg/24 hours). With 2+ spot urine albumin in 22 patients, 20 (90.9%) had significant proteinuria. All the patients (16) with spot urine albumin 3+ or 4+ had significant proteinuria.

12-Hours Urine Protein	24-Hours Urine Protein >300 mg (n=111)	24-Hours Urine Protein <300 mg (n=189)
>165 mg	107	8
<165 mg	4	181

Table 1. Correlation between 12-Hour Urine Protein and 24-Hour Urine Protein. (Total Number of Patients 300, 'n' is the Number of Patients in the Subgroup)

Category	24-hours Urine Protein <300 mg (n=189)	24-hours Urine Protein ≥ 300 mg (n=111)
24-hours urine protein mg, mean ± SD	192.96 ± 60.147 (86-298)	1078.65 ± 944.37 (312-3706)
12-hours urine protein mg, mean ± SD	103.47 ± 37.56 (40-188)	568.54 ± 516.858 (70-2390)

Table 2. Urine Collection Characteristics by 24-Hour Urine Protein Result

Urine Dipstick	Nil	Trace	1+	2+	3+	4+
24-hours urine protein <300 mg, (n=189)	152 (80.4%)	21 (11.1%)	14 (7.4%)	2 (1.1%)	0	0
24-hours urine protein ≥300 mg, (n=111)	30 (27%)	30 (27%)	15 (13.5%)	20 (18%)	14 (12.6%)	2 (1.8%)

Table 3. Urine Dipstick Results Categorised According to 24-Hour Urine Protein Result. (Total Number of Patients is 300, 'n' is the Number of Patients in the Subgroup)

Group	VS Group	Correlation Coefficient	p value
Spot urine albumin	24-hours urine protein	0.589	0.00
12-hours urine protein	24-hours urine protein	0.983	0.00

Table 4. Performance Characteristics of 12-Hour Urine Protein ≥165 mg and Spot Urine Albumin with 24-Hour Urine Protein

Variable	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
12-hours urine protein >165 mg	96.39%	95.76%	93.04%	97.83%
Spot urine albumin	45.94%	91.53%	76.11%	74.2%

Table 5. Performance Characteristics of 12-Hour Urine Protein ≥165 mg and Spot Urine Albumin with 24-Hour Urine Protein

DISCUSSION

Our study group included 300 patients with high blood pressure admitted in Institute of Maternal and Child Health, Kozhikode, during 1 year period from January 2013 to December 2013.

A 24-hour urine protein excretion ≥300 mg is taken as standard threshold for the diagnosis of pre-eclampsia among these patients.

The American College of Obstetrics and Gynaecology, the working group on hypertension in pregnancy of the National High Blood Pressure Education Program and the American Society of Hypertension, all list greater than 300 mg/day as defining proteinuria in pregnancy.[2]

First 12-hour urine sample was collected at the time of admission regardless of time of day and protein is quantitatively estimated. Urine dipstick for albumin was also done simultaneously.

A 12-hour urine protein cut off value was taken as 165 mg, because it was generated by Adelberg et al in a largest available study that had evaluated the 12-hour protein for the prediction of 24-hour urine protein estimation.[5]

115 patients showed 12-hour protein ≥165 mg (38.33%). Among patients with 24-hour urine protein more than 300, 107 patients had 12-hour urine protein ≥165 mg and 12-hour urine protein was falsely positive in 8 patients.

Sensitivity of 12-hour urine protein for the diagnosis of pre-eclampsia is 96.39% with positive predictive value of 93.04%, specificity 95.76% and negative predictive value of 97.83%. These observations were comparable to Christina Tun et al in a study to compare the 12-hour urine protein and protein creatinine ratio with 24-hour urine protein for the diagnosis of pre-eclampsia (96% sensitivity, 100% specificity, positive predictive value of 100% and negative predictive value 98%).[4]

Urine protein in 24-hour urine sample and 12-hour urine sample strongly correlate with p value <0.01 and r value 0.983. Similar findings were obtained in a study conducted by Rangasamy Savitha et al on replacing 24-hour albumin excretion with a shorter collection period in pre-eclampsia. Albumin concentration in 12-hour collection fitted closely with 24-hour urine collection with correlation coefficient of 0.98 and p value 0.0001.[6]

Patients who showed false-positive and false-negative 12-hour urine protein estimation has 24-hour urine protein values close to the diagnostic cut off. This finding is similar to findings by Adelberg et al. In their study, the specificity (97%), sensitivity (100%), positive predictive value (89%) and negative predictive value (100%) of 12-hour urine protein is more in severe proteinuria compared to mild disease. In mild proteinuria, sensitivity was 78%, specificity 100%, positive predictive value 100% and negative predictive value 71%.[5]

In a study published in AJOG by Christina Tun et al, a 12-hour urine protein ≥165 mg and protein:creatinine ratio of more than 0.15 correlated significantly with 24-hour urine protein ≥300 mg. A 12-hour urine protein ≥165 mg performed better than protein:creatinine ratio as a predictor of a 24-hour urine protein ≥300 mg.[4]

Based on the above-mentioned observations they concluded that the high correlation of 12-hour urine protein ≥165 mg with 24-hour urine protein ≥300 mg (with the benefit of a shorter evaluation time) and the high negative predictive value of protein:creatinine ratio suggest that the use of both these tests have a role in the evaluation and treatment of women with suspected pre-eclampsia.[7]

Rinehart et al in a 12-hour urine collection study to accurately assess the proteinuria came into the conclusion that 12-hour urine protein accurately depicts the amount of proteinuria in hospitalised gravidas being evaluated for pre-eclampsia, sensitivity of this method was 96% and specificity was 100%.[8]

So, based on observations of my study and the previous studies mentioned above, 12-hour urine-protein estimation has a role in the evaluation of pre-eclampsia with the benefit of shorter evaluation time.

Spot Urine Dipstick Albumin and 24-hour Urine Protein- 67 patients had spot urine albumin 1+ or above and was nil/trace in 233 patients. Of the 233 patients with spot urine albumin nil/trace, 173 (74.24%) had no significant proteinuria (<300 mg/24 hours), while 60 patients (25.75%) had proteinuria ≥300 mg/24 hours. 29 patients in the study had spot urine albumin 1+ of which only 15 (51.72%) had significant proteinuria (≥300 mg/24-hours). With 2+ spot urine albumin in 22 patients, 20 (90.9%) had significant proteinuria. All the patients (16) with spot urine albumin 3+ or 4+ had significant proteinuria.

There is moderate positive correlation present between urine spot albumin and 24-hour urine protein with r value 0.589 and p value 0.000. But, strength of this test as a diagnostic test is poor with sensitivity of 45.94%, specificity of 91.53%, positive predictive value 76.11% and negative predictive value of 74.2%.

In our study, accuracy of spot urine albumin maybe improved at a higher thresholds (greater than 2+). But, available data are sparse and thus it is not possible to make a meaningful inference about accuracy at a higher urine dipstick thresholds.

The correlation of the dipstick with the 24-hour excretion of protein was studied by Meyer et al. A 1+ dipstick has a 92% positive predictive value to predict >300 mg of protein. However, a negative to trace dipstick result does not rule out proteinuria and up to 66% of these patients will have ≥300 mg of protein in a 24-hour urine collection.[3]

In a study by Phalen et al, dipstick proteinuria was significantly more likely to be correct (true positive/true negative) if diastolic blood pressure was elevated >90 mmHg ($p = 0.032$) and in the absence of ketonuria ($p = 0.001$). Accepting a diagnosis of pre-eclampsia on the basis of de novo hypertension and dipstick testing alone was accurate less often (70%) when >1+ was used as a discriminant value than at the 82% of presentations when >2+ was used ($p = 0.001$).[9] In a study conducted by Gangaram et al, 198 women who presented with hypertension in pregnancy assessed the accuracy of urine dipsticks as a screening test for proteinuria in hypertensive disorders of pregnancy and noted that the positive predictive value for dipstick analysis ranged from 64.9% (single voided sample) to 94.2% (24-hour urine aliquot) and negative predictive value ranged between 75.2% to 84.2%. Hence, he concluded that dipstick analysis is not accurate.[10]

In a study conducted by Kieler H et al on which sample to be used in assessing urinary albumin excretion in pre-eclamptic women concluded that spot urine samples were inaccurate and were not recommended for quantification of albumin excretion.[11]

So, uniformly, the dipstick has received very poor press as many studies have shown that a negative, 1+ (30 mg/dL) and even 2+ (100 mg/dL) reading is associated with substantial false positives and negatives. The major problem with a qualitative dipstick measurement of course relates to one of the kidneys cardinal functions, concentration and dilution of urine. For instance, in face of polyuria and extremely dilute urine, a dipstick value of trace or even negative can be associated with excessive protein excretion.

Based on our observations and these former studies, 12-hour protein estimation can be recommended as a diagnostic test for pre-eclampsia and urine dipstick method cannot be used as a diagnostic test for pre-eclampsia.

CONCLUSION

1. The high correlation of 12-hour urine protein >165 mg with 24-hour urine protein ≥300 mg suggest that use of this test has a role in the evaluation of women with suspected pre-eclampsia and could be substituted for 24-hour urine protein as a simple, faster and cheaper method.
2. Spot urine albumin has a moderate positive correlation with 24-hour urine protein, but strength of this test as a diagnostic test is poor with low sensitivity, specificity, positive and negative predictive value, hence not recommended for quantification of albumin excretion.

Acknowledgement- The authors would like to thank the Department of Obstetrics and Gynaecology and administration of Government Medical College, Kozhikode, Kerala, for permission to study and providing facility to carry out the work.

REFERENCES

[1] Robert JM, August PA, Bakris G, et al. Task force on hypertension in pregnancy- practice. ACOG 2013:17-79.

[2] Cunningham FG, Leveno KJ, Bloom SL, et al. Pregnancy hypertension. Chapter 34. In: Williams Obstetrics. 23rd edn. McGraw Hill Medical publications 2009:706-756.

[3] Meyer NL, Mercer BM, Friedman SA, et al. Urinary dipstick protein: a poor predictor of absent or severe proteinuria. Am J Obstet Gynecol 1994;170(1 Pt 1):137-141.

[4] Tun C, Quiñones JN, Kurt A, et al. Comparison of 12-hour urine protein and protein:creatinine ratio with 24-hour urine protein for the diagnosis of pre-eclampsia. Am J Obstet Gynecol 2012;207(3):233.e1-8.

[5] Adelberg AM, Miller J, Doerzbacher M, et al. Correlation of quantitative protein measurements in 8-, 12- and 24-hour urine samples for the diagnosis of pre-eclampsia. Am J Obstet Gynecol 2001;185(4):804-807.

[6] Rangasamy S, Rao AJ. Replacing 24-hour urine albumin excretion with a shorter collection period in pre-eclampsia. Journal of Obstetrics and Gynaecology of India. 2012;62(4):424-428.

[7] Waugh JJ, Clark TJ, Divakaran TG, et al. Accuracy of urinalysis dipstick techniques in predicting significant proteinuria in pregnancy. Obstet Gynecol 2004;103(4):769-777.

[8] Rinehart BK, Terrone DA, Larmon JE, et al. A 12-hour urine collection accurately assesses proteinuria in the hospitalized hypertensive gravida. J Perinatol 1999;19(8 Pt 1):556-558.

[9] Gangaram R, Ojwang PJ, Moodley J, et al. The accuracy of urine dipsticks as a screening test for proteinuria in hypertensive disorders of pregnancy. Hypertens Pregnancy 2005;24(2):117-123.

[10] Lindheimer MD, Kanter D. Interpreting abnormal proteinuria in pregnancy: the need for more pathophysiological approach. Obstet Gynecol 2010;115(2 Pt 1):365-375.

[11] Kieler H, Zettergren T, Svensson H, et al. Assessing urinary albumin excretion in pre-eclamptic women: which sample to use? BJOG 2003;110(1):12-17.