

Diagnostic Accuracy of Spot Urinary Protein: Creatinine Ratio for Quantification of Proteinuria in Hypertensive Pregnant Women

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ABSTRACT

Objective: To determine the diagnostic accuracy of spot urinary protein-creatinine ratio keeping 24 hours urinary protein as gold standard in hypertensive pregnant women. **Design:** Cross Sectional Analytical Study. **Place and Duration of Study:** Department of Obstetrics and Gynaecology, Fatima Memorial Hospital, Lahore during July 2009 to December 2009. **Patients and Methods:** Urine collection for 24 hours was performed in 101 pregnant women with hypertensive disorders of pregnancy. Protein-creatinine ratio in spot urine sample was determined keeping 24 hours urinary protein as gold standard. Sensitivity, specificity, false positive and false negative rate along with diagnostic accuracy was calculated from data. **Results:** Sixty five of the included women were recorded positive on the basis of twenty four hour urinary protein > 0.30 mg/dl cutoff. The protein creatinine ratio on the basis of cutoff value 0.33, detected 50 cases as positive. The sensitivity of protein creatinine ratio was found 73.8%, and specificity was 94.4%. The diagnostic accuracy was found to be 81.2%. **Conclusion:** Random spot protein creatinine ratio is accurate, reliable and steadfast, time saving test for diagnosis of preeclampsia and it can substitute 24hours urinary protein excretion estimation in clinical practice.

Key Words: spot protein: creatinine ratio, 24 hours urinary protein, hypertension.

INTRODUCTION

Proteinuria is a major indicator of hypertensive disorder of pregnancy and also one of the diagnostic criteria of its severity.¹ Patients with hypertension have only <300mg proteinuria, those with mild pre-eclampsia have 300mg to 500mg and those with severe pre-eclampsia have >5000mg of urine protein in 24 hours.²

The gold standard for diagnosis of significant proteinuria is 24-hour urine collection in patients with hypertensive disorders of pregnancy³. However, it is time consuming, cumbersome, subject to collection error, and is difficult to administer on out patients⁴. The 24 hours period required for collection of urine may result in a delay in diagnosis and treatment or possibly a prolonged hospital stay.

In recent years, random urinary protein-creatinine ratio has been suggested as a rapid test for prediction of 24-hour protein excretion.² A close correlation have seen exist between the protein-to-creatinine ratio in random urine samples and the 24-hour protein excretion measured by 24-hour urine collection.⁵ Protein/creatinine ratio of a single voided urine specimen may have a role in the management of ambulatory women with suspected PIH, which necessitates further research in this field.⁶ The main potential benefit of this method is that in institutions where women with suspected PIH are hospitalized, women with insignificant proteinuria may be identified within a matter of hours and their follow-up care handled on an outpatient basis.

The aim of this study was to evaluate the diagnostic value of protein-creatinine ratio in single voided urine samples for quantification of

proteinuria correlate to those of a 24 hours sample in patients with pre-eclampsia.

PATIENTS AND METHODS

This cross sectional analytical study was carried out in indoor department of Gynae Unit-2, Fatima Memorial Hospital, Lahore, during the period of July 2009 to December 2009. The hospital ethical committee approved the study. A total 101 pregnant women with hypertensive disorders and who were >20 week of gestation were recruited in the study. Blood pressure more than 140/90 mmHg or a positive dipstick test of a value + (>300mg) or more for proteinuria made them candidate of study.

Patients of chronic hypertension, renal disease, autoimmune disease, urinary tract infection and pathological vaginal discharge were excluded. Patients who required delivery before completion of 24 hours urinary sample were also excluded.

Patients were advised to pass urine at 8:00am (as per standard protocol to discard early morning sample) and collect all the urine subsequently till 8:00am next morning (24 hours period). Protein and creatinine ratio was measured from random sample of urine after the 24 hours collection was over (to discriminate the particular sample for urinary protein:creatinine ratio) in all same patients after giving them instructions. Each container was labeled with the patient's name, serial number, and collection time. Sample sent to laboratory. Both tests were done on urine analyzer Selectra_E of Merck Company.

The collected information was entered and analyzed by using SPSS 15.0. The qualitative variables like parity, age group, gestational age group and positive and negative cases were presented by frequencies or percentages. The quantitative variables like age, gestational age, 24 hour protein excretion, and spot urinary protein: creatinine ratio was reported by using mean \pm SD, median and ranges were also given.

The measurement of 24-h protein excretion was used as gold standard and sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy for spot urinary protein: creatinine ratio were given along standard errors and 95% confidence intervals.

RESULTS

This was a cross sectional analytical study. A total of 101 consecutive parturient with new onset of hypertension were identified and followed for results. The average age for these women was 29.9 ± 5.1 years with a median age of 29 years and range 19–39 years. The average gestational age was 32.8 ± 4.4 weeks with median of 33 weeks and range 22–40 weeks. Of these women 44.6% were nulliparous (Table 1).

Table 1: Demographic characteristics of study group.

Parameters	Number	Percent
Age (Years)		
19 - 24	19	5.9
25 - 30	31	12.9
31 - 35	35	26.7
36 - 39	16	11.9
Total	101	100
Gestational age		
< 28	7	6.9
28 - < 31	21	20.8
31 - < 34	40	39.6
34 - < 37	21	20.8
37 or more	12	11.9
Total	101	100.0
Parity		
Primigravida	45	44.6
Multigravida	56	55.4

The mean protein level was 1.34 ± 0.6 g with a median of 1.8 (range 0.1–8.2) in 24 hours urine collection. Twenty one patients (20.8%) had a 24-hours protein excretion of 2 g or greater, and only one patient had a 24-hour protein excretion of 5 g or greater.

The mean protein: creatinine ratio was 0.36 ± 0.14 g with a median of 0.33 (range 0.0 – 0.6) in 24 hours urine collection. Fifty patients (49.5%) had a protein: creatinine ratio of greater than 0.33.

Sixty five of the included women were recorded positive on the basis of twenty four hour urinary protein > 0.30 mg/dl cutoff. The protein creatinine ratio on the basis of cutoff value 0.33 (was verified from ROC curve also), detected 50 cases as positive. The sensitivity of protein: creatinine ratio

was found 73.8%, and specificity was 94.4%. The diagnostic accuracy was found to be 81.2% (Table 2).

Table 2: Sensitivity, specificity, positive, negative predictive value and diagnostic accuracy of urinary spot protein:creatinine ratio.

Pre-eclampsia	Number	Percent
True positive	48	47.52
False positive	02	1.98
True negative	34	33.66
False negative	17	16.83
Total	101	100

Sensitivity	= 73.8%,
Specificity	= 94.4%,
Positive Predictive Value	= 96.0%,
Negative Predictive Value	= 66.7%,
Diagnostic Accuracy	= 81.2%

DISCUSSION

In the present study, we primarily investigated the ratio of significant proteinuria in a group of consecutive patients with hypertensive disorders of pregnancy. The negative predictive value of random urine protein-creatinine ratio was high and did not vary greatly with an increasing cutoff point of protein-creatinine ratio for significant proteinuria detection. We chose a cutoff point (> 0.33) that minimized the false positive ratio while maintaining high sensitivity. With use of this cutoff point, the test had a good negative predictive value (66.7%) in excluding significant proteinuria. However, the positive predictive value of the test was only 96.0%, and a test result above the cutoff point was diagnostic for significant proteinuria.

The random protein-creatinine ratio can be used in serial testing with 24-hour urine collection in mild hypertensive disorders of pregnancy. For a patient with a positive random urinary protein-to-creatinine ratio, proceeding with collection of a 24-hour urine sample seems a reasonable option.

The diagnostic accuracy of the protein/creatinine ratio in the prediction of proteinuria was investigated in 2 recent studies. A high negative predictive value is available in both studies for patients with a low prior probability of

disease. With a cutoff of 0.19 or greater, Rodriguez-Thompson and Lieberman reported a sensitivity of 91% and a specificity of 70%¹². Durnwald and Mercer reported a sensitivity of 91% and specificity of 48% with a cutoff point of 0.20¹³. Using Bayes' theorem, given a prior probability of 21% for significant proteinuria, a negative predictive value of 97% was estimated from the study of Rodriguez-Thompson and 95% from that of Durnwald and Mercer.^{12, 13}

In their novel study, Ginsberg et al. proposed that random urine protein-creatinine ratio provides a good estimation of total protein excretion per 24 hours, when glomerular filtration was stable and urinary creatinine and protein excretion was assumed to be fairly constant.¹⁴ Then, the 24-hour protein excretion rate could be estimated by the concurrent rate of creatinine excretion. Their study did not include pregnant women. Protein excretion rates, however, can vary from hour to hour in preeclampsia.

Sethuram et al. assesses the diagnostic value of protein creatinine ratio in preeclampsia by correlating it to 24-hour urinary protein. There sensitivity was 83% and specificity 92% that is comparable to our study¹⁵. A similar study was conducted in pathology department of Chandka Medical College Hospital, Larkana. Their results showed that relationship of random urine protein creatinine ratio and 24-hour urinary protein excretion is highly significant and positive in mild to severe proteinuria but not significant in massive proteinuria¹⁶.

Cote MA et al did a systematic review; thirteen studies were reviewed for spot protein creatinine ratio and albumin creatinine ratio as diagnostic test for significant proteinuria in hypertensive pregnant women. They made the conclusion that spot urine protein creatinine ratio is a reasonable "rule out" test for significant proteinuria of 0.3g/dl or more in pregnancy¹⁷. Thomas et al conducted a similar study in pre-eclamptic women. They also found strong correlation of random spot protein creatinine ratio with 24-hour urinary protein levels (Pearson r = 0.88) kept cutoff 0.21 (300mg/24hour) and 3.0 (5000mg/24hour).¹⁸ Rahman MM et al also obtained similar results in non diabetic chronic renal disease patients¹⁹.

Our study that spot protein creatinine ratio is an alternative test to 24-hour urinary protein collection which is cumbersome, time consuming, inconvenient and subject to error due to inaccurate timings and/or incompleteness. The method of detection of proteinuria with random protein creatinine ratio is faster and within safe limits to aid diagnosis and in early start of treatment hence ensuring better fetomaternal outcome. Also many studies have stressed on early detection and prompt management of patients with proteinuria that is beneficial for patient and fetus^{21,22}.

CONCLUSION

In conclusion, random urine protein-creatinine ratio is a good predictor of significant proteinuria in hypertensive disorders of pregnancy and can replace the 24-hour urine collection as a diagnostic test. The spot protein creatinine ratio is reliable, relatively faster and accurate for proteinuria so shortening the period of diagnosis of preeclampsia would be valuable for treatment purpose as well as decreasing the hospital cost and patient inconvenience. Earlier diagnosis ensures good fetomaternal outcome.

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