Original Article

Diagnostic Accuracy of Spot Urine Protein-Creatinine Ratio in Women with Pre-Eclapmsia

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ABSTRACT

Objective: To determine the diagnostic accuracy of spot urine protein-creatinine ratio in women with pre-eclampsia as compared with 24-hr urine protein excretion.

Study Design: Descriptive / cross-sectional study

Place and Duration of Study: This study was conducted at Obstetrics and Gynecology Department of Liaquat University Hospital, Hyderabad for duration of one year from February 20, 2015 to February 19, 2016.

Materials and Methods: Subjects for this study were collected by using non-probability consecutive sampling technique Women of all parity having systolic blood pressure (SBP) ≥140 mmHg or a diastolic BP (DBP) ≥90 mmHg were included for this study. Women with medical disorders like renal disease, diabetes mellitus, were excluded.

Information regarding demographic data, medical history, obstetrical history, general physical examination and ultrasonography were recorded. A spot mid-stream urine sample was obtained from every patient afterthat 24-hour urine collection was started. Patients having confirmed proteinuria were considered and treated for pre-eclampsia. All information were recorded on a predesigned proforma. SPSS version 16.0 was used for data analysis.

Results: Total 404 pregnant hypertensive women were included in this study. The mean±SD age of the subjects was 27.08±5.84 years. The mean±SD systolic blood pressure of the subjects was 161.68±19.59 mmHg, whereas the mean±SD diastolic blood pressure of the subjects was 104.70±12.65 mmHg on dipstick test 140 (34.7%) presented with 1+. The results of 24-hours urine collection showed that 158 (39.1%) subjects were negative for proteinuria while urine protein-creatinine ratio revealed that 358 (88.6%) subjects were positive for preeclampsia

Conclusion: The present study indicates that for the clinical purposes, spot urine protein-creatinine ratio is a satisfactory and reliable substitute for determination of proteinuria than in a 24 hour urine collection.

Key Words: Preeclampsia; proteinuria; protein-creatinine ratio; 24h urine collection; sensitivity; specificity; diagnostic accuracy

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INTRODUCTION

Hypertension complicating pregnancy along with hemorrhage and infection are one of the deadly triad that contributes to the major proportion of maternal death and disability.[1,2] Hypertension in pregnancy with proteinuria is known as pre-eclampsia[3] The worldwide incidence of pre-eclampsia is 10%[4] and it is responsible for 15% of all direct maternal deaths[5].

In Pakistan the reported rate of maternal death due to pre-eclampsia and eclampsia is about 11.7%[6].

Preeclampsia is diagnosed when woman is having raised blood pressure of 140/90 or higher after 20-weeks of gestation along with proteinuria.[7,8] Proteinuria is a significant component of pre-eclampsia and defined as 300-mg or more excretion of protein per 24-hrs[9].

When proteinuria is overt and persistent, then the risk of maternal and fetal morbidities increases. Hence the quick and error free detection and measurement of proteinuria is essential for the management and prevention of complication in pregnant women with preeclampsia. In pregnancy protein measurement in the 24-hour urine sample is used as a traditional standard method[10.] But recent studies suggested that this Gold standard method is inconvenient and costly besides this it can delay the clinical diagnosis and may prolong the hospital stay[11]. Therefore an alternative method has been considered that is protein-creatinine ratio[12]. The correlation between spot protein-creatinine ratio and 24-hour urine protein excretion has been reported significant with p-value up to 0.001[13].

The protein-creatinine ratio in a single urine specimen has been used for rapid and accurate detection of proteinuria.[14]

It avoids collection error and gives physiologically more relevant information. Hence, there is a need to evaluate these tests which can be used to overcoming the limitations of routinely performed tests[15].

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Lot of data is available from western part of world where patients may have different genetics and available diagnostic resources are very much advanced. Very scare data is available from low resource countries like Pakistan The purpose of is to determine the diagnostic accuracy of spot urine protein-creatinine ratio, as compared to conventional 24-hr urine protein excretion. The results of this study may aid in saving resources and time.

MATERIALS AND METHODS

This was a descriptive cross-sectional study. This study was carried out at Obstetrics and Gynecology Department of Liaquat University Hospital, Hyderabad. The duration of this study was one year from February 20, 2015 to February 19, 2016.

Sampling Technique: Subjects for this study were collected by using non-probability consecutive sampling technique.

Sample Size: Sample size was calculated by taking the P=10% and d=7%, with 95% confidence interval, spot urine protein-creatinine sensitivity 92%[13] and specificity 88%[13]. Thus, the sample size calculated was 404 cases of pregnant hypertensive Patients.

Inclusion Criteria: Women of all parity with more than 20-weeks gestation according to dating ultrasonograph presenting with systolic blood pressure (SBP) ≥140 mmHg or a diastolic BP (DBP) ≥90 mmHg were selected for this study.

Exclusion Criteria: Women presenting with ruptured membranes and those who delivered during urine collection period were excluded from the study. Women with urinary tract infection and other associated medical disorders like renal disease, diabetes mellitus, women who had bed-rest longer than 24-hours at presentation were not included.

Data Collection: An informed consent was obtained from women who fulfill the inclusion criteria. All information regarding demographic data, medical history, obstetrical history, general physical examination and ultrasonography were recorded. A spot mid-stream urine sample was obtained from every subject and protein creatinine ratio of 0.20 was set as cut off point, immediately after which 24-hour urine collection was started i.e. from 08:00 a.m. to 08:00 a.m. next morning. Total protein concentration was measured by biuret colorimeter assay and creatinine level was measured by modified Jaffe test. Protein-creatinine ratio in urine was obtained by dividing the urinary protein concentration by urine creatinine concentration. Subjects having confirmed proteinuria were considered and treated for pre-eclapmsia. All information was recorded on a predesigned Proforma.

Data Analysis: Relevant descriptive statistics, frequencies and percentages were calculated for quantitative data like presence of hypertension, proteinuria and parity. Mean with standard deviation were calculated for continuous data like age, parity, systolic blood pressure, diastolic blood pressure, 24-hr urinary protein excretion.

The diagnostic accuracy of the spot urine protein-creatinine ratio was obtained by sensitivity, specificity, PPV and NPV calculated by their respective standard formulae by using 2x2 table; taking 24-hr urinary protein excretion ≥300-g as gold standard for comparison. SPSS version 16.0 was used for data analysis. All results are presented in the form of frequency distribution tables.

RESULTS

Total 404 pregnant hypertensive patients were included in this study. The demographic details of the patients were given in table 1 The mean±SD age of the women was 27.08±5.84 years and range was from 16-years to 40 years. 86 (21.29%) women in age group of up to 20 years, 223 (55.2%) and 95 (23.51%) women were age group of 21-30 years and 31-40 years respectively.

Twenty-three (5.69%) patients presented with gestational age of 20-25 weeks, 33 (8.19%) were at the gestational age of 26-30 weeks, while 61 (15.1%) and 287 (71.04%) were presented at 31-35 weeks and >35-weeks of gestational age respectively. The mean±SD gestational age of the subjects was 36.26±4.59 weeks.

Among 404 patients 84 (20.8%) were primiparous, 221 (54.7%) were multiparous and 99 (24.5%) were grand-multiparous

Majority 248(61.4%) of the patients belongs to rural areas. While only 156 (38.6%) patients were from urban areas. Table 1.

Table No.I: Demographic data (n=404)

Age Group	**Number**	**Percentage**
≤20 years	86	21.29
21-30 years	223	55.20
>30 years	95	23.51
Mean±SD age=	27.08±5.84 years	
Gestational Age		
20-25 weeks	23	5.69
26-30 weeks	33	8.19
31-35 weeks	61	15.1
>35 weeks	287	71.04
Mean±SD gestational age = 36.26±4.59 weeks.		
Parity		
Primiparous (para 1)	84	20.8
Multiparous (para 2-5)	221	54.7
Granmultiparous	99	24.5
Area of Residence:		
Rural	248	61.4
Urban	156	38.6

Data is presented as numbers and percentages

The mean±SD systolic blood pressure of the patients was 161.68±19.59 mmHg, whereas the mean±SD diastolic blood pressure was 104.70±12.65 mmHg.

On the urine dipstick 106 (26.2%) patients presented with traces of protein urea, 140 (34.7%) presented with 1+ while 94 (23.3%) and 64 (15.8%) presented with 2+ and 3+respectively.

Table No.2: Blood Pressure readings and values of three methods used for detection of Proteinuria (n=404)

Blood Presure	**Mean**	**SD**
Systolic Blood Presure (mmHg)	161.68	19.59
Diastolic BloodPresure (mmHg)	104.70	12.65
Dipstick Values		
Value	**Number**	**Percentage**
Traces	106	26.2
1+	140	34.7
2+	94	23.3
3+	64	15.8
Preeclampsia according to 24-h urine collection protein		
PROTEINURIA		
Negative	158	39.1
Positive	246	60.9
Preeclampsia according to protein-creatinine ratio		
Proteinuria	**Number**	**Percentage**
Negative	46	11.4
Positive	358	88.6
Mean±SD protein-creatinine ratio = 1.23±1.58		

Data is presented as numbers and percentage

Table No.3: Diagnostic accuracy of Protein-Creatinine ratio (n=404)

		24-h Urine Collection Protein		
		True	False	Total
Protein-Creatinine Ratio	Positive	240	118	358
	Negative	6	40	46
	Total	246	158	404

Sensitivity = TP/(TP+FN) = 240/246 = 0.975
Specificity = TN/(TN+FP) = 40/158 = 0.253
PPV = TP/(TP+FP) = 240/358 = 0.670
NPV = TN/(TN+FN) = 40/46 = 0.869

The results of 24-hours urine collection showed that 158 (39.1%) women were negative for proteinuria and 246 (60.9%) women were positive for proteinuria i.e. they presented with >300-mg protein. The mean±SD protein in 24-hours urine collection was 1447.06± 2045.27-mg.

The results of protein-creatinine ratio showed that 46 (11.4%) women were negative for preeclampsia and 358 (88.6%) women were detected positive for preeclampsia the mean±SD protein-creatinine ratio was 1.23±1.58. As given in table 2

The Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value of protein-creatinine ratio was 97.5%, 25.3%, 67% and 86.9% respectively, as detailed in Table 3

DISCUSSION

Pre eclampsia is differentiated from gestational hypertension by the presence of significant proteinuria. An accurate and quick detection of proteinuria is important not only for the management of Preeclampsia but also for prevention of complications related with the severity of the disease.

The gold standard for the diagnosis of significant proteinuria remains the 24-hours urine protein. A 24-hr collection is need there is high degree of variation in the urine protein concentration during the course of the day. Though the method of 24 hours urine collection was considered as Gold standard but it is time consuming and can be inaccurate because of incomplete collection.

For these reasons simpler methods which can measure urinary protein in spot samples like urinary dipstick and urine protein-creatinine ratio are proposed and we evaluated it in present study.

Consistent with many previous reports[16,17] the present study indicated positive and significant correlation of urine protein-creatinine ratio with 24-hour urine result.

One study conducted by Sethuram et al. they asses the diagnostic value of protein creatinine ratio in preeclmpsia by correlating it to 24hour urinary protein. There sensitivity was 83% and specificity 92% it is similar to our study.[18] Another similar study was conducted Chandka Medical College Hospital, Larkana. There results indicated that relationship of random urine protein creatinine ratio and 24hour urinary protein excretion is very much significant and positive in mild to severe proteinuria but it is not significant in massive proteinuria.[19]

a systematic review; done by Cote MA et al, they reviewed thirteen studies for spot protein creatinine ratio and albumin creatinine ratio as diagnostic test for significant proteinuria in women with Hypertension during pregnancy. The conclusion of that review was that spot urine protein creatinine ratio is a reasonable "rule out" test for significant proteinuria of 0.3g/dl or more in pregnancy[20]. Similarly Thomas et al conducted a similar study in pre-eclamptic women. They also found significant correlation of random spot protein creatinine ratio with 24hour urinary protein levels.[21]

The present study indicated that a urine Protein/ Creatinin ratio of 0.20 corresponded with a protein excretion rate of 300 mg/24 h. these findings were Consistent with literature. We also detected a strong

correlation (r = 0.84) between the spot P/C ratio and the 24-hour urine protein similar to literature[16-17]. But there are some reports with conflicting results. The variation in results could be due to different reasons like the variation in laboratory methods for detection of proteinuria, use of different cutoff points and different units for the urinary P/C ratio[22].

In one study by Durnwald and Mercer[23], the authors reported a poor correlation between the random urinary P/C ratio and the 24-hour urine total protein and they advised against replacing the spot P/C ratio for the 24-hour urine protein collection. The variation of findings between their report and ours may be due to the difference in the study population and the wider exclusion criteria in our population may explain the higher positive and negative predictive values. Furthermore, the patient recruited in their study were from outpatient Department, who could have incomplete urine collections, which may be associated with lower levels of 24-hour urine total protein that increases the false negative rate[23].

Our results indicated that the random urine P/C ratio is a highly accurate test for differentiating between insignificant and significant proteinuria. The key concern regarding clinical use of this test is the false-negative results, as 8% of patients with preeclampsia may be missed.

To obtain the optimal cutoff, we suggest that while increasing specificity one need to maintain a sensitivity of higher than 90% this will be reducing the possibility of missing the diagnosis of preeclampsia.

The present study have some limitation we need further Research in the future s focusing on the evaluation of clinical outcomes and the cost-effectiveness of the use of a random urinary P/C ratio for prediction of significant proteinuria. In addition, studying the test in an outpatient basis should be further considered in order to apply it in ambulatory management of preeclamptic patient. We suggest that the test be done also in severely preeclamptic women, as they tend to excrete greater amounts of protein, in order to determine a cutoff value for prediction of the 24-hour urine protein excretion of greater than 5 g.

CONCLUSION

The present study indicates that this method for quantification of proteinuria, when properly interpreted, and validated by laboratory can provide valuable information regarding diagnosis and severity of the disease. Hence for the clinical purposes, spot urine protein-creatinine ratio is a satisfactory and reliable substitute for determination of proteinuria than in a 24 hour urine collection.

Conflict of Interest: The study has no conflict of interest to declare by any author.

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