

STUDY OF PROTEIN/CREATININE RATIO IN PREECLAMPSIA AS AN ALTERNATIVE TO 24 HOURS URINE PROTEIN IN MANIPAL TEACHING HOSPITAL OF NEPAL

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ARTICLE INFO

Article History

Received : 14 February 2018

Accepted : 25 March, 2018

Published : 30 April, 2018

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ORA 54

DOI: <http://dx.doi.org/10.3126/bjhs.v3i1.19756>

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Citation

Shrestha P. Study of Protein/creatinine Ratio in Preeclampsia as an Alternative to 24 Hours Urine Protein in Manipal Teaching Hospital of Nepal. BJHS 2018;3(1)5 : 350 - 353.

ABSTRACT

Introduction

Hypertensive disorder in pregnancy complicates around 5 to 10% of all pregnancies. It is one of the leading causes of maternal and fetal morbidity and mortality. Measurement of protein excretion by 24 -hour urine protein collection is gold standard but as it is time consuming, an alternative method like random urine protein/creatinine ratio is required.

Objectives

The aim of this study was to assess the diagnostic accuracy of urine protein/ creatinine ratio compared with 24-hour urine protein as an alternative method for evaluating proteinuria in preeclampsia.

Methodology

Patients with preeclampsia after 20 weeks of gestation were included in the study. Random urine protein/ creatinine ratio and 24-hour urine for protein was collected and evaluated for proteinuria. Results were entered and analysis was done.

Results

Fisher's exact test depicted a positive association between UPCR with 24-hour urine protein, p value being less than 0.05. The area under curve was calculated as 0.87 95% CI (0.74-1.01), which was statistically significant. At cut off point of 0.3, sensitivity was 100%, specificity 90%, positive and negative predictive value 97.2% and 100% respectively.

Conclusion

Random urine protein/ creatinine ratio (≥ 0.3) is a reliable indicator of proteinuria $\geq 300\text{mg/day}$. It can be used as an alternative to 24-hour protein estimation.

KEYWORDS

Preeclampsia, pregnancy, proteinuria, urinalysis.

INTRODUCTION

Hypertension is diagnosed when systolic blood pressure is 140mm Hg or more and diastolic is 90mmHg or more after 20 weeks of gestation in a previously normotensive woman. Proteinuria is an objective marker that reflects endothelial leakage, which characterizes preeclampsia syndrome.

Hypertensive disorder in pregnancy complicates around 5 to 10 percent of all pregnancies. It is one of the deadly causes that contributes to maternal morbidity and mortality.¹

Hypertension and eclampsia accounts for 12 percent of maternal mortality in Nepal.²

The commonly performed techniques for estimating proteinuria are qualitative dipstick test, the quantitative 24-hour protein and protein/creatinine ratio of a single voided urine specimen. Abnormal protein excretion is defined as persistent dipstick 30mg/dl(1+), 24-hour urine protein exceeding 300mg and protein/creatinine ratio >0.3.¹ Urine dipstick test despite being easy to perform has low sensitivity and specificity and is influenced by various factors like maternal hydration, presence of the infection, exercise.³ Urine dipstick is a poor predictor of the 24-hour urine total protein level.^{4,5}

Estimation of 24-hour urinary protein though being gold standard needs admission, is time- consuming and may not be completed due to delivery. Therefore, an alternative technique Urine Protein/creatinine ratio (UPCR) may form a reliable alternative for proteinuria measurement.

Protein excretion may vary during different times of day but when divided by spot creatinine which is constant during the day, UPCR ratio forms a reliable indicator of proteinuria. It doesn't require admission, is convenient and reports are available fast thus helping for early planning.⁶

The aim of the study was to estimate the diagnostic accuracy of urine protein/creatinine ratio in predicting 300mg of proteinuria of protein/day in patients with preeclampsia.

METHODOLOGY

The study was conducted in the Department of Obstetrics and Gynaecology, Manipal Teaching Hospital, Pokhara, Nepal. Ethical approval was obtained from Institutional Review Committee (IRC) before the study was carried out. A total of 45 patients diagnosed with hypertension i.e. systolic blood pressure ≥ 140 mmHg and diastolic blood pressure ≥ 90 mmHg after 20 weeks of gestation with 1+dipstick or more in urine were included in the study. After obtaining random urine protein and creatinine concentration, the ratio was calculated by dividing protein concentration by creatinine concentration. The sample for 24-hour urine protein was collected in the container after discarding first voided morning sample. Thereafter from the same time till next 24 hours, patient was instructed to collect voided urine in a container. Final collected urine was incorporated into the total collected volume for measuring 24-hour protein. Result obtained was entered and analysis was done using

SPSS 16 and p-value ≤ 0.05 was considered statistically significant.

RESULT

Total of 45 pregnant ladies with preeclampsia was included in the study. Age of the patients ranged from 18 years to 39 years. Period of gestation was from 29 to 41 weeks. Of the total 45 patients, 55.5% of patients had less than 37 weeks of gestation. The majority (56%) of patients were primigravida. Mean uric acid was 5.6 ± 1.47 . The higher number of patients i.e, 55.6% had LSCS and 28.9% had preterm vaginal delivery, 13.3% had normal vaginal delivery and 2.2% had instrumental delivery. In this study, 53% of babies were born less than 2.5kg. Out of 45 babies, 14 babies (31%) required NICU admission and 2 babies (4.4%) were stillborn.

Table 1: Urine dipstick test

Urine dipstick	Frequency (%)
1+	16 (35.6%)
2 +	13 (28.9%)
3+	6 (13.3%)
4+	10 (22.2%)

Table1 shows distribution of patients according to urine dipstick. The higher percentage of of patients had 1+ Urine dipstick.

Table2. Association of Urine protein/creatinine ratio (UPCR) with 24-hour urine protein.

UPCR	24- hour protein (gm)						
	<0.3	0.3-0.9	1-1.9	2-2.9	3-3.9	4-4.9	≥ 5
<0.3	9	1	0	0	0	0	0
≥ 0.3	0	15	11	2	5	0	2

Table 2 shows the association of UPCR with 24 hours urine protein. Fisher's exact test depicted a value of 31.36 with p value 0.001 which is statistically significant.

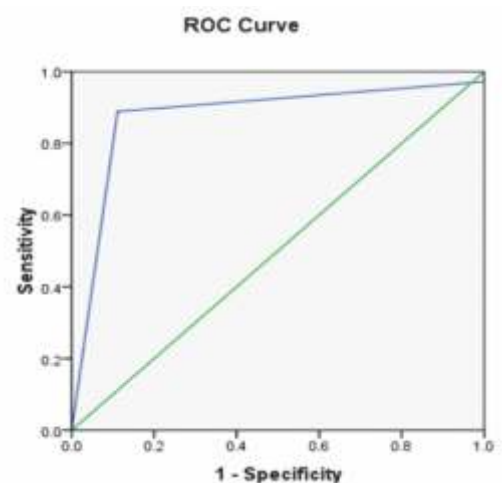


Figure 1: Receiver Operating Characteristic curve

Figure 1, indicates ROC curve for urine protein/creatinine ratio to predict 300mg proteinuria in 24 hours.

The area under curve was calculated as 0.87(95% CI (0.74-1.01), which was statistically significant.

Table 3: Urine protein/creatinine ratio (UPCR) to predict proteinuria of 300mg in 24 hours.

UPCR	<300 mg (n)	≥300 mg (n)	Total
<0.3	9	1	10
≥0.3	0	35	35

According to table 3, 90% of patients had urine protein less than 300mg when UPCR was less than 0.3. When UPCR was 0.3 or more all the patients had proteinuria of 300mg or more.

Table 4: Urine protein/creatinine ratio to predict proteinuria of ≥300mg/day.

Sensitivity	100%
Specificity	90.2%
Positive predictive value	97.2%
Negative predictive value	100%
Positive likelihood ratio	10
Negative likelihood ratio	0.0

At cut off point of 0.3, sensitivity was 100%, specificity 90%, positive and negative predictive value 97.2% and 100% respectively.

DISCUSSION

Hypertension in pregnancy has a significantly increased maternal and fetal morbidity and mortality. Proteinuria is a sign of preeclampsia which is defined as ≥300mg of protein in 24 hours. 24-hour collection of proteinuria is the gold standard in the diagnosis of preeclampsia but to avoid the time consumption in the collection, efforts have been made to find a faster method which correlates well with the standard method. A urine protein/creatinine ratio has been studied to be used as a reasonable alternative to 24-hour urine protein estimation.

In our study, Fisher's exact test depicted a positive association between Urine protein/creatinine ratio with 24-hour urine protein found ($p < 0.05$). There was a

significant correlation between 24-hour protein excretion and the urine protein/creatinine ratio ($r = 0.828$, $p < 0.0001$) in the study done by Kayatas S et al.⁷ Similar findings were noted in the study done by Kashinakunti SV et al.⁸

ROC curve for urine protein/creatinine ratio to predict ≥300mg proteinuria in 24 hours showed area under the curve as 0.87(95% CI (0.74-1.01), which demonstrated the test as an excellent test for detection of proteinuria. This study with sensitivity of 100% and specificity 90.2% allows obstetricians for prompt identification of cases with significant proteinuria. The study had positive predictive value, negative predictive value of 97.2% and 100% respectively. So this test will be useful in diagnosing proteinuria in patients with preeclampsia. The study conducted by Hossain S et al showed similar findings with sensitivity of 91.67%, specificity 80%, positive predictive value and negative predictive value of 88% and 85.71% respectively.⁹

However, the study done by Durnwald C et al, showed poor correlation of protein/creatinine ratio with 24-hour urine protein. It may be because of variation in gestational age, change of renal function over the course of hours.¹⁰

LIMITATION OF STUDY

Sample size was small.

CONCLUSION

The present study shows that spot urine protein/creatinine ratio is equally accurate as 24-hour urine protein estimation in patients with preeclampsia. Since it is a simple and fast test it helps in early diagnosis and management of patient with preeclampsia and thus can be used as a replacement test for 24 hour urine protein estimation.

RECOMMENDATION

A larger study would be recommended.

ACKNOWLEDGEMENT

None

CONFLICT OF INTEREST

None

Table 5: The diagnostic summary of different studies at UPCR of 0.3 as compared to present study is listed below.

Study	Sensitivity (%)	Specificity (%) curve(95%CI)	Area under	Positive likelihood ratio	Negative likelihood ratio
Present study	100	90	0.87	10	00
Sapna V Amin et al.2014. ⁶	89.7	54.2	0.89	6.56	0.21
Kumari et al.2013. ¹¹	90	84	0.83	5.65	0.12
Leanos-Miranda et al.2007. ¹²	98.2	98.8	0.99	79.3	0.02
Ramos et al.1999. ¹³	95	80	Not reported	4.75	16



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