Significance of Protein: Creatinine value in PIH

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Abstract
Objectives: To evaluate the significance of the urine protein to creatinine value in hypertensive pregnant patients.
Design: This is a single group comparison study of a single group of 240 subjects.
Setting: This study was conducted in the Department of OBG, JIPMER, Pondicherry, a tertiary care hospital south India, from April 2010 to March 2013.
Materials and Methods: Morning urine sample was sent for urine protein and creatinine value. Rest of the 24 hour urine collected and tested for 24-hour urine protein value.
Main Outcome Measures: The spot urine protein to creatinine value significantly correlates with 24-hour urine protein value. (r=0.98; P<0.0001). The protein to creatinine value for significant proteinuria was 0.285. The sensitivity was 100%. Specificity was 99. The positive predictive value 100%. Negative predictive value was 99%.
Results: The urine protein to creatinine value for significant proteinuria was 0.285.
Conclusion: The urine protein to creatinine value can be used as an alternative to 24 hour urine protein for clinical purposes.

Keywords: Protein to creatinine value, Hypertension in pregnancy.

Introduction
Hypertension in pregnancy complicate up to 10% of pregnant women. It is a major cause of maternal morbidity and mortality.1

Hypertension in pregnancy is a multisystem disorder of an unknown aetiology, with more than or equal to 140 mm of Hg systolic and 90mm of Hg diastolic Blood pressure, with proteinuria after 20 weeks of pregnancy in previously normotensive and non-proteinuric patients.1 If 300 mg or more of protein in a 24-hour urine specimen is considered as proteinuria in pregnancy.2

One complete day urine collection method is cumbersome. It has so many for protein errors. Most obvious error is variable and complete collection is difficult. It may be inconvenient for many patients. There are incidences of delay in availability of results. Patient may deliver before the arrival of results. Difficulty in arranging storage and staff inadequacy are added problems. Admission of patient for the test itself is burden to hospital.

Urine protein to creatinine value may be a good solution for the above mentioned problems. Since it has shown good results and showed comparable reports with the 24-hour urine protein.3-5 So urine protein to creatinine value can be used as an alternative to 24 hour urine protein for clinical purposes.

Aims and Objectives
To evaluate the significance of the urine protein to creatinine value in hypertensive pregnant patients.

Materials and Methods
This study was conducted in the Department of OBG, JIPMER, Pondicherry, a tertiary care hospital south India, from April 2010 to March 2013.

It consists of 240 patients of single group. This is a comparative study. Calculation of sample size was done by using the standard formula for estimating the sensitivity of a new test. It was estimated with a sensitivity of urine protein to creatinine value for significant proteinuria as 95%, with a 5% of level of significance and 4% precision.

Inclusion Criteria
Pregnant women who have completed 20 weeks of gestation with hypertension of 140/90 mmHg or higher on two occasions, at least 6 hours apart, were included in the study.

Exclusion Criteria
Patient’s renal problems and diabetics were excluded. Even patients suffering from urinary tract infections also taken out from the study.

Every patients details like demographic profile, gestational age, blood pressure, urine protein to creatinine value and 24-hour urine protein values were studied. The patient had been informed with proper explanation in native language. They were enrolled after their consent for the test.

Morning urine sample was sent for urine protein and creatinine value. Rest of the 24 hour urine collected and tested for 24-hour urine protein value.

Urine protein value obtained by the colorimetric method. The modified Jaffé’s method was used for urine creatinine value estimation with a standard auto analyser. The sensitivity, specificity, and positive and negative predictive values were calculated for different protein to creatinine value. Receiver operating characteristic (ROC) curves were used for comparisons.

Results
Total recruited patients were 240. Twenty seven delivered
before completion of urine collection. Twenty three patients urine collection was incomplete. Seven patients discontinued. Urinary tract infection was found in 7 patients. Therefore 64 patients excluded from the study at initial step only. Remaining 176 patients were studied and followed up to 6 weeks. Seven patients turned out to be chronic hypertension. One hundred sixty nine patients were studied finally.

The patients age ranged from 18 years to 39 years. Majority 131(87.51%), of them were 20-30 years. Sixty five (39%) patients were of gestational hypertension group. Pre-eclampsia patients were 100(59%) and eclampsia patients were 4(2%).

Ninety patients (53.25%) were primigravida were as 79(46.75%) multigravidas. It showed similarity in both groups. Average gestational age was between 30 and 36 weeks in 88(52.07%) patients. Standard investigations were performed in all cases as per the patients clinical scenario.

Only one patient had body mass index less than 18 where as the majority, 108(63.91%) of them had body mass index values between 26 and 30.55. Body mass index of more than 35 was found in 9 patients. Past history of pre-eclampsia was found in 11 patients. One hundred forty three patients required antihypertensive drugs. Antepartum steroids given for lung maturity of fetus in 42 patients. Around 40 patients required magnesium sulphate.

Induction of Labour was done in 136 patients. There were 99(59%) term deliveries. Seventy (41%) of them were preterm deliveries. One hundred fifty six singleton pregnancies. Sixteen were twin gestation. Around 3 were triplets. There was one case of single fetal demise. One hundred and thirty eight (70%) were low birth weight babies. Forty-six (25.14%) newborns were transferred to the neonatal intensive care unit. Intrauterine foetal death was occurred in 10(5%) of cases. Ten (5%) were still births. Intrauterine growth retardation seen in 15.38% of patients.

Non significant proteinuria was found in 102(59%) of cases and 67(40%) had significant proteinuria (≥ 300 mg/day). During follow up 7 patients found to be chronic hypertension cases.

There is a good correlation found between the spot urine protein to creatinine value (mg/mg) and the 24-hour urine protein (mg/mg)

The area under the ROC curve is 0.999 (95% confidence interval). The protein to creatinine value for significant proteinuria was 0.285. The sensitivity was 100%. Specificity was 99. The positive predictive value 100%, Negative predictive values was 99%.

**Discussion**

In the present study there is a good correlation found between the spot urine protein to creatinine value (mg/mg) and the 24-hour urine protein (mg/mg) with P value of <0.0001 (two tailed), and an excellent correlation coefficient (r=0.9778), with a 95% confidence interval of 0.9700 to 0.9836, for the spot urine protein to creatinine value (mg/mg) and 24-hour urine protein (mg/day) calculated by Pearson’s method (Table 1).

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>P value (two tailed)</th>
<th>95% confidence interval</th>
<th>Correlation coefficient (r)</th>
<th>Coefficient of determination (r2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>169</td>
<td>&lt;0.0009</td>
<td>0.9700-0.9836</td>
<td>0.9778</td>
<td>0.9561</td>
</tr>
</tbody>
</table>

The coefficient of determination found to be 0.9561. Table 2 shows the results of previous studies in comparision with present study.

**Table 2: Comparision of present study with previous studies**

<table>
<thead>
<tr>
<th>Studies</th>
<th>Correlation coefficient</th>
<th>P-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ginsberg et al.6</td>
<td>0.93</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Neithardt et al.7</td>
<td>0.93</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Robert et al.8</td>
<td>0.94</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Boler et al.9</td>
<td>0.99</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Saudan et al.3</td>
<td>0.93</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Young et al.10</td>
<td>0.80</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Jaschevatzy et al.11</td>
<td>0.92</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Present study</td>
<td>0.98</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

ROC curves for the spot urine protein to creatinine ratio show an area under the ROC curve of 0.999(95% confidence interval)

The significant value of 0.285 results in a sensitivity of 100%, specificity of 99.02%, positive predictive value of 99%, and negative predictive value of 100%, with a 67% likelihood ratio.
Conclusion
Proteinuria in pregnancy has considerable clinical importance outcome of pregnancy. For the course of pregnancy and the perinatal and maternal outcomes. So early detection with preventive measures will have greater impact on maternal and neonatal health.

Commonly used Dipstick analysis lacks reliability. False positives results are more with this test. One complete day urine collection method is cumbersome. It has so many for protein errors. Most obvious error is variable and complete collection is difficult. It may be inconvenient for many patients. There are incidences of delay in availability of results. Patient may deliver before the arrival of results. Difficulty in arranging storage and staff inadequacy are added problems. Admission of patient for the test itself is burden to hospital.

Urinary protein to creatinine value may be a good solution for the above mentioned problems. Since it has shown good results and showed comparable reports with the 24-hour urine protein.3-5 So urinary protein to creatinine value can be used as an alternative to 24 hour urine protein for clinical purposes.

Random sample assessment is more convenient. It will be more acceptable to the patients. In hypertensive disorders of pregnancy investigations needs to be repeated often too. Practically waiting for one day for report is also not a good option. So random sample assay appears to be good option.

The value of urinary protein to creatinine is 0.285 mg protein/mg creatinine is considered for significant proteinuria. If value lower than 0.285 need not be associated with significant proteinuria. Hence further testing can be avoided. It can provide valuable information if interpreted properly for clinical purposes and is a satisfactory substitute for 24-hour protein estimation.

Limitations
The present study has limitation of hospitalised patients who were non-ambulatory patients. Proteinuria will be affected by postural changes. So it may be a confounding factor in the quantitation of proteinuria.

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Conflict of Interest: None.

References

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