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ORIGINAL ARTICLE

Spot Urinary Albumin-to-Creatinine Ratio: A Novel Marker for Detecting Fetomaternal Outcomes and Complications in Preeclamptic Women

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Abstract

Introduction Preeclampsia is a multisystem endothelial disease leading to glomeruloendotheliosis with endothelial leak causing significant proteinuria. It is associated with high maternal and fetal risks and fetomaternal morbidity and mortality. Spot urinary albumin-to-creatinine ratio (ACR) leads to earlier detection of glomerular damage leading to prompt management of preeclamptic patients.

Aims and Objectives To study the correlation between fetomaternal outcomes of preeclamptic patients with spot urinary ACR.

Materials and Methods Spot urinary ACR was measured in 70 consecutive patients with preeclampsia in Assam Medical College, Dibrugarh. The best cutoff value to differentiate between significant and insignificant proteinuria was calculated. Mean spot urinary ACR was calculated in all maternal outcomes (mode of onset of labor and mode of delivery), and maternal complications (elevated liver enzymes, renal insufficiency, severe hypertension, coagulation disturbances and thrombocytopenia, antepartum and postpartum hemorrhage) and fetal complications and outcomes (birth weight, Apgar score, IUGR, need for resuscitation, NICU requirement, neonatal sepsis, jaundice and mortality) and the correlation were studied.

Results The best cutoff value to differentiate significant and insignificant proteinuria was calculated as 291.9 mg/g beyond which adverse fetomaternal outcomes and complications were seen. All maternal and fetal outcomes and complications had high mean spot urinary ACR and were found to be significant ($p < 0.05$). Mode of delivery and birth weight of babies showed no statistical significance though low-birth-weight babies had high mean spot ACR.

Conclusion Compared with 24-h urinary protein excretion, spot urinary ACR is a simple and accurate indicator of significant proteinuria and helps to detect fetomaternal outcomes in preeclamptic women which may lead to prompt management to reduce fetomaternal complications.

Keywords Spot urinary albumin to creatinine ratio (ACR) · Preeclampsia · 24-h urinary protein

Introduction

Preeclampsia is determined by the presence of blood pressure ≥ 140/90 mm Hg on two occasions at least 4 h part in a woman with previously normal blood pressure and significant proteinuria defined as the excretion of ≥ 300 mg of protein in a 24-h urine collection or a timed excretion that is extrapolated to this 24-h urine value or a protein-to-creatinine ratio of at least 0.3 (each measured as mg/dL) or a urinary dipstick of 1 + (recommended only if sole test available) after the 20th week of gestation [1].

Preeclampsia is a significant contributor of maternal and fetal mortality, and it affects 2–8% of all pregnancies worldwide. Worldwide about 76,000 pregnant women die each

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year from preeclampsia and related hypertensive disorders. Hypertensive disorders along with sepsis (10.7%) are the second most leading cause of maternal mortality after hemorrhage (27.1%) [2]. Fetal deaths due to maternal hypertensive disorders are thought to be in the order of 500,000 per annum. According to WHO [3], the burden of preeclampsia lies more over developing countries and up to a maximum of 25% results in maternal death.

According to NICE guidelines [4], one of the cornerstones of detection of preeclampsia includes blood pressure measurement and urine analysis for the detection and quantification of significant proteinuria which is essential for diagnosis and assessment of severity of the disease. A need exists for a simple, rapid, convenient and accurate test to identify significant urinary proteinuria. This may lead to a timely decision-making aimed to decrease the patient's anxiety, reduce both fetal and maternal complications, shorten the length of hospital stay with its associated cost savings and detect women with true pathology for treatment.

A consensus has not yet been reached on spot urinary ACR's use in the detection of fetomaternal outcomes and complications.

Aims and Objectives

To study the fetomaternal outcomes and their association with 24-h urinary protein and spot urinary ACR.

Materials and Methods

This was a prospective hospital-based study at Assam Medical College and Hospital, Dibrugarh, conducted for a period of 1 year (June 2016 to June 2017) on a sample size of 70. Approval was obtained from the Institutional Ethics Committee.

Inclusion Criteria

1. Primigravida with singleton pregnancy with cephalic presentation with intact membranes.
2. Patients having blood pressure recording of 140/90 mm Hg or more on two occasions 4 h apart or a single diastolic reading of more than or equal to 110 mm hg after 20th week of pregnancy and the presence of proteinuria $\geq 1+$ as detected by dipstick urine analysis.
3. All booked and unbooked cases willing for a hospital delivery at Assam Medical College and Hospital Dibrugarh.

Exclusion Criteria

1. Women with previous renal disease, chronic hypertension, urinary tract infection, gestational diabetes, connective tissue disorders, epilepsy and pathological vaginal discharge.
2. Women who developed eclampsia.
3. Women who required delivery before completion of 24-h urine sample for any reason whatsoever.
4. Cases who would have incomplete 24-h urine collection and proteinuria < 300 mg would be excluded.
5. Patients not giving written informed consent.
6. Patients lost to follow-up.

Methodology

A total of 70 consecutive participants depending upon inclusion and exclusion criteria were selected. Upon willingness to participate in the study, they were provided with a written and informed consent. A special pro forma was made and filled for every patient who had given full and valid consent to participate in the study. Elaborate history was taken, and examination was done for every patient in the study. For all cases, routine investigations and special investigations like dipstick test for urine albumin in random urine sample, 24-h urinary protein, spot urinary albumin-to-creatinine ratio, liver function tests, renal function tests, coagulation profile, etc., were done.

Evaluation of Proteinuria

For all patients, screening of proteinuria was performed by urinary dipstick method followed by 24-h urine collection which was started from 8 am in the morning following admission and was taken till next morning 8 am and was sent to the Department of Pathology at AMCH, Dibrugarh.

Following this, 5–10 mL midstream voided urine sample was collected for calculating spot urinary albumin-to-creatinine ratio immediately after the 24-h urine collection. This sample was sent to a NABL laboratory nearby AMCH, Dibrugarh. This was made free of cost to the patient.

Results

The study aimed at determining the association between 24-h urinary protein and spot urinary ACR and fetomaternal outcomes (Table 1).

Table 1 Tests of validity of spot urinary ACR (at 300 mg/g) in the prediction of significant proteinuria (=300 mg/day)

Spot urinary ACR (mg/gm)	24-Hour urinary protein (mg/day)		Total
	≥300	<300	
≥300	57	2	59
<300	3	8	11
Total	60	10	70
Sensitivity	95%		
Specificity	80%		
PPV	96.6%		
NPV	72.7%		

The sensitivity of the two tests showed that spot urinary ACR at 300 mg/gm had a better sensitivity of 95% and specificity of 80%. The PPV was 96.6%, and NPV was 72.7% (Table 2).

Maximum number of patients underwent induction of labor and had a normal vaginal delivery. The mean spot urinary ACR was found to be higher in patients who had received labor induction as compared to those who had a spontaneous onset of labor, higher in patients with a preterm live birth and intrauterine fetal demise as compared to the patients who had a full-term live birth and higher in those patients who underwent an emergency cesarean section and an elective cesarean section in comparison with the patients who underwent a normal vaginal delivery and an assisted vaginal delivery. The relation between mean spot urinary ACR and type of labor and outcome of pregnancy was found to be statistically significant. The relation between mean spot urinary ACR and mode of delivery was found to be statistically insignificant (Table 3).

The relation between severe hypertension, renal insufficiency, raised liver enzymes, thrombocytopenia, coagulation disturbances and postpartum hemorrhage in relation to mean spot urinary ACR was found to be statistically significant. Thus, there was an increased risk of adverse maternal complications with higher mean spot urinary ACR (Table 4).

Patients who delivered newborns with birth weight less than 2.5 kg had a slightly higher mean spot urinary ACR in comparison with those with normal birth weight. Overall, the relation between birth weight of the newborn and mean spot urinary ACR was found to be statistically insignificant.

The relation between intrauterine growth restriction, Apgar score at 1 min and 5 min, need for resuscitation and NICU admission and spot urinary ACR was found to be statistically significant (Table 5).

The relation between neonatal mortality and mean spot urinary ACR was found to be statistically significant. The relation between neonatal jaundice and sepsis, respectively, with mean spot urinary ACR was found to be statistically insignificant.

Discussion

The present study has been comparable to previous studies in many aspects. In the present study, the most discriminant value for spot urinary albumin-to-creatinine ratio for detecting significant proteinuria (≥300 mg/day in a 24-h urine collection) was found to be 291.9 mg/gm which yielded a sensitivity of 98.33% and a specificity of 80%. The result of the present study was similar to that found in the latest study by Shreya et al. [5], Kayatas et al. [7] and Huang et al. [8] in terms of the best cutoff value of spot urinary albumin-to-creatinine ratio to detect significant proteinuria (Table 6).

In the present study, it was observed that various maternal complications like severe hypertension, renal insufficiency, raised liver enzymes, thrombocytopenia, coagulation

Table 2 Maternal outcomes

Maternal outcome parameters	Total		Spot urinary ACR (mg/gm)			*p* Value*
	n	%	Mean	SD	Range	
Type of labor						
Spontaneous	26	37.14	796.3	593.70	182.8–2492.4	*p* value < 0.05
Induced	39	55.71	2453.0	957.21	1291.7–4940.7	
LSCS (elective)	5	7.14	2100.5	1261.58	194.7–3180.7	
Mode of delivery						
Normal vaginal delivery	47	67.14	1710.2	1177.00	182.8–4940.7	*p* value = 0.614
LSCS (elective)	5	7.14	2100.5	1261.58	194.7–3180.7	
LSCS (emergency)	14	20.0	2081.5	1169.73	451.9–4334.5	
Assisted vaginal delivery	4	5.71	1712.5	1067.86	288.8–2572.2	
Outcome of pregnancy						
Full-term live birth	31	44.29	1245.2	1040.39	182.8–3308.1	*p* value = 0.002
Preterm live birth	33	47.14	2292.0	1119.60	695.1–4940.7	
IUD	6	8.57	2105.5	720.42	1424.2–2901.6	

Table 3 Maternal complications

Maternal complication parameters	Total	Spot urinary ACR (mg/gm)				*p* Value*
	N	%	Mean	SD	Range	
Severe hypertension (BP ≥ 160/110 mmHg)						
Present	9	12.86	3663.4	663.20	2982.2–4940.7	p value < 0.05
Absent	61	87.14	1539.4	951.82	182.8–3474.2	
Renal insufficiency (S. creatinine > 1.1 mg/dL)						
Present	13	18.57	3409.2	683.62	2599.4–4940.7	p value < 0.05
Absent	57	81.43	1448.3	915.58	182.8–3474.2	
Raised liver enzymes (transaminase levels)						
Present	26	37.14	2884.5	900.02	755.4–4940.7	p value < 0.05
Absent	44	62.86	1178.9	769.56	182.8–2901.6	
Thrombocytopenia ($< 150 \times 10^9$/L)						
Present	13	18.57	3437.7	688.42	2492.4–4940.7	p value < 0.05
Absent	57	81.43	1441.8	900.42	182.8–3308.1	
Coagulation disturbances						
Present	9	12.86	3663.4	663.20	2982.2–4940.7	p value < 0.05
Absent	61	87.14	1539.4	951.82	182.8–3474.2	
Antepartum hemorrhage						
Present	1	1.43	4334.5	–	–	–
Postpartum hemorrhage						
Present	6	8.57	3190.5	357.16	2683.3–3667.7	p value = 0.001
Absent	64	91.43	1683.2	1128.00	182.8–4940.7	
No cases of pulmonary edema and maternal mortality						

Table 4 Fetal outcomes

Fetal outcome parameters	Total		Spot urinary ACR (mg/gm)			*p* Value*
	n	%	Mean	SD	Range	
Birth weight (kg)						
< 2.00	4	5.71	2519.9	1691.56	1285.2–4940.7	p value = 0.148
2.00–2.49	44	62.86	1958.0	1074.75	194.5–4334.5	
2.5–2.99	15	21.43	1223.8	1261.27	182.8–3667.6	
≥ 3.00	7	10.00	1754.7	873.71	288.8–2683.3	
IUGR						
Yes	24	34.29	2388.8	951.29	940.2–4334.5	p value = 0.003
No	46	65.71	1511.7	1145.30	182.8–4940.7	
APGAR at 1 min						
≤ 7	36	51.43	2400.8	1002.13	695.1–4940.7	p value < 0.05
> 7	34	48.57	1189.5	991.71	182.8–4077.4	
APGAR at 5 min						
≤ 7	15	21.43	2477.1	992.00	1328.9–4940.7	p value = 0.011
> 7	55	78.57	1631.2	1147.04	182.8–4334.5	
Need for resuscitation						
Yes	27	38.57	2491.5	1038.04	1281.8–4940.7	p value < 0.05
No	43	61.43	1386.1	1034.85	182.8–4077.4	
NICU admission						
Yes	13	18.57	3417.6	714.48	2424.7–4940.7	p value < 0.05
No	57	81.43	1446.3	906.30	182.8–3180.7	

Table 5 Fetal complications

Fetal outcome parameters	Total		Spot urinary ACR (mg/gm)			*p* Value*
	n	%	Mean	SD	Range	
Congenital malformation						
Yes	1	1.43	1496.4	–	–	–
Neonatal jaundice						
Yes	2	2.86	1926.8	704.14	1428.9–2424.7	*p* value = 0.777
No	68	97.14	1809.1	1176.49	182.8–4940.7	
Neonatal sepsis						
Yes	4	5.71	2026.7	815.60	1285.2–2982.2	*p* value = 0.723
No	66	94.29	1799.5	1183.66	182.8–4940.7	
Neonatal mortality						
Present	4	5.71	3398.7	1083.64	2424.7–4940.7	*p* value = 0.018
Absent	66	94.29	1716.3	1102.87	182.8–4334.5	

Table 6 Comparison of tests of validity between 24-h urinary protein and spot urinary ACR with that of other studies

Study	24-h urinary protein cutoff (mg/day)	Spot urinary ACR cutoff value (mg/gm)	Sensitivity (%)	Specificity (%)
Huang et al. [8]	300	228	82.4	99.4
Kayatas et al. [7]	300	280	60.4	77.8
Shreya et al. [5]	300	200	91.2	87.8
Present study (2016–2017)	300	291.9	98.33	80

disturbances, antepartum hemorrhage and postpartum hemorrhage were associated with higher mean spot urinary albumin-to-creatinine ratio in the mother. Demirci et al. [9] have also reported that adverse maternal outcomes like severe hypertension, renal insufficiency, liver dysfunction and thrombocytopenia increase with increasing spot urinary protein-to-creatinine ratio. Similarly, Nischintha et al. [10] found three maternal complications—abruptio placentae, intrapartum eclampsia and HELLP syndrome in patients with significant proteinuria detected by high spot urinary protein-to-creatinine ratio.

Women who delivered babies with birth weight < 2 kg had higher values of spot urinary ACR in the mother. Newborns with low Apgar scores at 1 and 5 min had higher values of spot urinary ACR in the mother. The present study also reported that various neonatal outcomes and complications like IUGR, requirement of resuscitation at birth, requirement of NICU admission and neonatal mortality were associated with higher mean spot urinary ACR in the mother. Neonatal complications like neonatal sepsis and neonatal jaundice were associated with lower mean spot urinary ACR in the mother. In a similar study, Chan et al. [11] have also reported adverse fetal outcomes like small for gestational age babies and neonatal mortality to increase with increasing spot urinary protein-to-creatinine ratio.

Conclusion

Diagnosing proteinuria and its correlation with fetomaternal outcomes and complications in preeclampsia by 24-h urinary protein estimation is a frustrating task for the obstetrician due to a long delay for results. Alternative testing methods like spot urinary albumin-to-creatinine ratios or spot urinary protein-to-creatinine ratios have been correlated well with this gold standard method, and the risk of adverse maternal and fetal outcomes was found to increase with higher values of spot urinary ACR.

Hence, the spot urinary ACR is a reliable, faster and accurate method for the detection of proteinuria in preeclampsia and may allow better management of women with preeclampsia, thereby decreasing maternal as well as perinatal morbidity and mortality, especially in low-resource settings and developing countries like India. This test could be used as an alternative to 24-h urinary protein estimation in the detection of significant proteinuria and better prediction of maternal and fetal outcomes in women with preeclampsia. However, the cost of ACR has been a deciding factor of its usage in low-resource countries like India and usage of 24-h urinary protein continues to be the deciding factor for the diagnosis of preeclampsia. However, further studies on a larger population may be required to consolidate the findings of the study.

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