



Spot Urinary Albumin Creatinine Ratio as a Predictor of Preeclampsia

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Abstract

Background: The current study has been designed to evaluate the usefulness of spot urinary albumin:creatinine ratio as a predictor in pregnant women.

Methods: A hospital based prospective study done on 625 women who attended the department of Obstetrics and Gynaecology, SMS Medical College, Jaipur from routine antenatal case, over a period of 1 year (June 2018 to May 2019) between 17-20 week of gestation were included in the study after obtaining informed consent.

Results: ROC curve to predict preeclampsia. A statistical software found that the area under the curve is 0.971 with SE = 0.024 and 95% CI from 0.923 to 1.00. The best cutoff that maximizes (sensitivity + specificity) is 25.32. At this, the sensitivity is 0.95 and specificity is 0.993 (1—specificity = 0.007).

Conclusion: A spot ACR in mid-stream urine might be considered a replacement of 24 h urine protein excretion in the evaluation of preeclampsia and

eclampsia. This test also has the potential to replace urinary dipstick method in routine antenatal clinic, but more data are required. It appears that ACR could be very useful test in near future not only for predicting the development of preeclampsia.

Keywords: ACR, Preeclampsia, Urine.

Introduction

Pre-eclampsia is best described as a pregnancy-specific syndrome that can affect virtually every organ system and although it is much more than simply gestational hypertension and proteinuria, appearance of proteinuria remains an important diagnostic criterion. Thus proteinuria is an objective marker and reflects the system-wide endothelial leak, which characterizes the preeclampsia syndrome.¹

Proteinuria is an important sign of preeclampsia, and diagnosis is questionable in its absence. It develops late in the course of the disease. As proteinuria increases, the likelihood of complications also increase, hence a rapid and accurate detection and quantification of

proteinuria is essential for the management of hypertensive pregnant women.

Studies have shown that urinary dipstick is a poor predictor of the 24-hour urine total protein level²⁻³ Compared with a qualitative dipstick result, a quantitative analysis of a random urine sample is necessary. As creatinine excretion is fixed and albumin concentration in urine varies with hydration status, the random (spot) urine albumin creatinine ratio (ACR ratio) nullifies the effect of hydration on protein estimation and gives physiologically more relevant information than 24 hour excretion method. Random urine sample collection is simple procedure and can be done at any time of the day, though few studies recommend morning samples.⁴ Early diagnosis of preeclampsia with a albumin and creatinine ratio would be a valuable diagnostic tool with good accuracy when albumin creatinine ratio > 0.3 The ratio of albumin to creatinine in a random "spot" urine can provide a rough estimate of protein excretion; for example, an albumin/creatinine ratio of 3.0 correlates to ~3.0g of proteinuria per day. It could prevent unnecessary hospitalization, testing, and lead to earlier diagnosis. Several authors have studied the relationship between the albumin/creatinine ratio and it has been found it to be superior diagnostic tool compared to routine urine analysis.

The current study has been designed to evaluate the usefulness of spot urinary albumin:creatinine ratio as a predictor in pregnant women.

Material & Methods

Study Population

A hospital based prospective study done on 625 women who attended the department of Obstetrics and Gynaecology, SMS Medical College, Jaipur from routine antenatal case, over a period of 1 year (June 2018 to May 2019) between 17-20 week of gestation

were included in the study after obtaining informed consent.

Sample Size

The sample size was calculated as 625 subjects at 80% study power & α -error of 0.05 assuming 2.4% incidence of preeclampsia in study group and AUC of ROC 0.87 as per study of Dr. Gupta N et al (Journal of Obstetrics and Gynaecology July-August 2017).

Inclusion Criteria

- Singleton pregnancy
- Gestational age between 17-20 wks by last menstrual period verified by USG.
- Urine sample provided at gestational age 17-20 wks.
- Normal renal function and no evident proteinuria upon measurement with dipstick.

Exclusion Criteria

- Multi-fetal pregnancy
- Women with hematuria, dipstick-positive proteinuria, ongoing urinary tract infection, acute renal failure or chronic kidney disease.
- Mental retardation or other mental disorder that doubts regarding the subject's true willingness to participate in study.
- Gestational age below 17 and above 20 wks by last menstrual period verified by USG.
- Lack of urine sample at the specified enrollment period.
- Known major fetal anomaly and fetal demise.
- Lack of demographic data.

Methods

All pregnant women of 17 to 20 week of Gestation attending Antenatal Department at SMS Medical College, Jaipur were selected according to inclusion and exclusion criteria as per sample size after written

& informed consent. Detailed History, General and systemic examination and routine blood investigations were carried out.

Urine sample irrespective of time was collected. Urine was tested for albumin and creatinine. Value of albumin to creatinine ratio was found out. Then at each visit subjects, were evaluated by eliciting history for symptom of preeclampsia and imminent eclampsia such as oedema, vomiting, epigastric pain, decreased urinary output and visual disturbance. Blood pressure was measured. The patients were followed up till delivery and association between albumin and creatinine ratio (ACR) and preeclampsia was found out. A mid stream clean catch spot urine sample was collected for estimation of albumin and creatinine. Albumin was determined by Immunoturbidimetric method and creatinine estimated by Jaffes’s method.

Estimation of Urinary Albumin

It was measured in spot urine sample by micro albumin turbidimetric procedure using micro albumin reagent and Beckman coulter AU analyzer. Results automatically printed out for each sample in mg/dl at 37 degree Celsius.

During operation of the Beckman coulter AU analyzer at least two levels of an appropriate quality control material of human origin only should be tested a minimum of once a day.

Expected Values

| Urine | 24-h collection (mg/24h) | Timed collection (µg/min) | Spot collection (µg/mg creatinine) |
|----------------------|--------------------------|---------------------------|------------------------------------|
| Normal | <30 | <20 | <30 |
| Microalbuminuria | 30-299 | 20-199 | 30-299 |
| Clinical Albuminuria | ≥300 | ≥200 | ≥300 |

Estimation of Urinary Creatinine

Urine creatinine was measured in spot urine sample by Modified Jaffe's reaction using Erba reagent kit at fully automated Beckman Coulter AU680. Urine was diluted 1/20 with distilled water and results were multiplied by 20. Daily control was run at auto analyzer.

Calculation

The creatinine value of the unknown is determined by comparing its absorbance change with that of a known standard.

$$\frac{Mg}{dl} = \frac{\Delta Abs(Unknown)}{\Delta Abs(Standard)(mg/dl)} \times \text{Concentration of Std.}$$

$$Mg/dl = \Delta Abs(Unknow) \times \text{Concentration of Std.}$$

$$\Delta Abs(Standard)(mg/dl)$$

Where: ΔAbs = Absorbance change between reading(A2-A1)

Estimation of Urinary Albumin Creatinine Ratio

Urine albumin was analyzed in mg/dl and urine creatinine was also analyzed in mg/dl in spot urine sample, urinary ACR was analyzed by simply dividing the urine albumin (mg/dl) by urine creatinine (mg/dl).

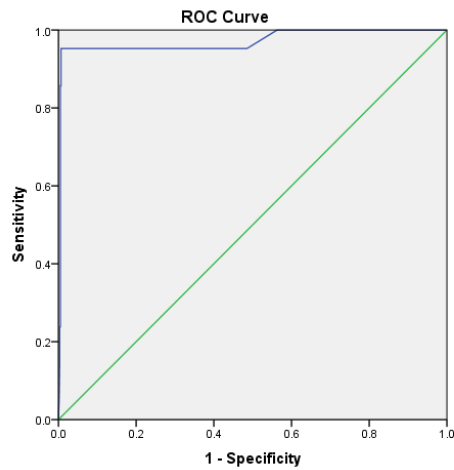
$$\text{Urinary ACR} = \text{Urine Albumin} / \text{Urine Creatinine}$$

Statistical Method

Comparison of spot urinary albumin creatinine ratio and birthweight between unaffected and affected groups was performed by Kruskal–Wallis test. ANOVA and Chi-square test were used for comparison of continuous and categorical data between the groups. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) at different values of urinary albumin creatinine ratio were calculated using receiver operating curve (ROC).

Results

Prediction of Preeclampsia by Estimating Urinary Albumin/Creatinine Ratio-



ROC curve to predict preeclampsia . The ROC curve obtained by plot at different cutoffs is shown in above figure. A statistical software found that the area under the curve is 0.971 with SE = 0.024 and 95% CI from 0.923 to 1.00. The best cutoff that maximizes (sensitivity + specificity)25.32. At this, the sensitivity is 0.95 and specificity is 0.993 (1—specificity = 0.007)

Area Under the Curve

Test Result Variable(s): Ratio

| Area | P value | 95% Confidence Interval | |
|------|---------|-------------------------|-------------|
| | | Lower Bound | Upper Bound |
| .971 | .000 | .923 | 1.000 |

AUC (area under curve)- 0.971

At cut off value of Urinary Albumin/Creatinine Ratio for Prediction of Preeclampsia – ≥ 25.32

| Urinary Albumin/Creatinine Ratio | Preeclampsia | | |
|----------------------------------|--------------------|---------------------|-------|
| | yes | no | Total |
| ≥ 25.32 | 20 (True Positive) | 4 (False Positive) | 24 |
| < 25.32 | 1 (False Negative) | 600(True Negative) | 601 |
| Total | 21 | 604 | 625 |

| Statistic | Value | 95% CI |
|---------------------------|--------|------------------|
| Sensitivity | 95.24% | 76.18% to 99.88% |
| Specificity | 99.34% | 98.31% to 99.82% |
| Positive Predictive Value | 83.33% | 65.20% to 93.03% |
| Negative Predictive Value | 99.83% | 98.88% to 99.98% |
| Accuracy | 99.20% | 98.14% to 99.74% |

The AUC value of the ROC curve showed that Urinary Albumin/Creatinine Ratio is a significant predictor for the development of preeclampsia, as a value of 0.971 shows an excellent accuracy (P<0.001).

A spot urinary albumin-to-creatinine ratio of more than 25.32 can predict the development of preeclampsia in later pregnancy with the sensitivity and specificity of 95.24% and 99.34% respectively.

Discussion

Hypertensive disorders in pregnancy stand out to be one of the leading causes of maternal and neonatal morbidity and mortality. Timely and effective intervention has utmost importance in the prevention of these complications. Proteinuria has been an important constituent of preeclampsia. Preeclampsia remains a leading cause of maternal and fetal morbidity and mortality. Studies have shown that alteration in the regulation and signaling of angiogenic pathway contributes to the inadequate cytotrophoblast invasion, resulting in preeclampsia. Endothelial dysfunction has been demonstrated as early as 22 weeks of gestation, and levels of antiangiogenic factors start rising as early as 17 weeks of gestation. It could be expected that microalbuminuria, a marker of endothelial dysfunction,

might also be apparent by this time.⁵In our study sensitivity and specificity was obtained from the ROC curve. The optimum spot urinary Albumin to creatinine ratio to predict preeclampsia was ≥ 25.32 which had a sensitivity of 95.24% and specificity of 99.34%. The area under curve was 0.971 (95%CI), PPV 83.33%, NPV 99.83%, P value 0.0001. In Gupta N. et al⁶ study the sensitivity and specificity of spot urinary Albumin to creatinine ratio was also obtained from the ROC curve. The area under curve was 0.879 with 67% sensitivity and 76% specificity. These results were similar to Mishra VV. et al⁷ study with cut value of 35.5. They analyzed a sensitivity of 87.5, specificity 96.30%, PPV 77.78% and NPV 98.10% for prediction of preeclampsia. In Baweja S. et al⁸ study, optimum spot urinary ACR which can predict preeclampsia was 35.8 which had a test sensitivity of 83.3%, specificity of 61.2%, PPV of 63% and NPV of 78.6%, which was also similar to our study.

Conclusion

A spot ACR in mid-stream urine might be considered a replacement of 24 h urine protein excretion in the evaluation of preeclampsia and eclampsia. This test also has the potential to replace urinary dipstick method in routine antenatal clinic, but more data are required. It appears that ACR could be a very useful test in the near future not only for predicting the development of preeclampsia.

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