Uric Acid as a Predictor of Adverse Maternal and Perinatal Outcomes in Women Hospitalized With Preeclampsia

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Abstract

Objective: Elevated serum uric acid is commonly observed in women with preeclampsia, but its utility in predicting adverse outcomes has recently been disputed. Our goal was to analyze data from a large cohort of women with preeclampsia to determine the utility of serum uric acid in predicting adverse maternal and perinatal outcomes.

Methods: Data were obtained from an ongoing international prospective study of women admitted to hospital with preeclampsia (Pre-eclampsia Integrated Estimate of RiSk). Univariate logistic regression was used to determine the relationship between serum uric acid concentration (both absolute and gestational-age corrected [*Z* score]) and adverse outcomes (maternal and perinatal). Analyses were conducted to compare cohorts of women with preeclampsia as defined by hypertension and proteinuria versus hypertension and hyperuricemia.

Results: Uric acid *Z* score was associated with adverse perinatal outcome (OR 1.5; 95% CI 1.4 to 1.7) and had a point estimate > 0.7 (area under the curve receiver operating characteristic 0.72; 95% CI 0.69 to 0.74). Serum uric acid concentration also showed a significant association with adverse maternal outcomes, but the point estimate was < 0.7. No significant differences were observed between groups in which preeclampsia was defined by hypertension and proteinuria and by hypertension and hyperuricemia.

Conclusion: In women admitted to hospital with preeclampsia, the serum uric acid concentration, corrected for gestational age via a *Z* score, is clinically useful in predicting adverse perinatal outcomes but not maternal outcomes.

Key Words: Preeclampsia, pregnancy outcome, risk assessment, uric acid

Competing Interests: None declared.

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Résumé

Objectif : Bien qu'un taux sérique élevé d'acide urique soit couramment constaté chez les femmes qui présentent une prééclampsie, son utilité pour ce qui est de la prévision des issues indésirables a récemment été remise en question. Nous avions pour objectif d'analyser les données issues d'une importante cohorte de femmes présentant une prééclampsie, afin de déterminer l'utilité du taux sérique d'acide urique pour ce qui est de la prévision des issues indésirables maternelles et périnatales.

Méthodes : Les données ont été tirées d'une étude prospective internationale toujours en cours qui porte sur des femmes hospitalisées présentant une prééclampsie (*Pre-eclampsia Integrated Estimate of RiSk*). Une régression logistique univariée a été utilisée pour déterminer la relation entre la concentration sérique en acide urique (tant absolue que corrigée en fonction de l'âge gestationnel [score Z]) et les issues indésirables (maternelles et périnatales). Des analyses ont été menées pour comparer des cohortes de femmes présentant une prééclampsie définie par l'hypertension et la protéinurie à des cohortes de femmes présentant une prééclampsie définie par l'hypertension et l'hyperuricémie.

Résultats : Le score Z quant à l'acide urique était associé à des issues périnatales indésirables (RC, 1,5; IC à 95 %, 1,4 - 1,7) et comptait une estimation ponctuelle > 0,7 (surface sous la courbe

de la fonction d'efficacité de l'observateur, 0,72; IC à 95 %, 0,69 - 0,74). Une association significative a également été constatée entre la concentration sérique en acide urique et des issues indésirables maternelles; toutefois, l'estimation ponctuelle était < 0,7. Aucune différence significative n'a été constatée entre les groupes « prééclampsie définie par l'hypertension et la protéinurie » et « prééclampsie définie par l'hypertension et l'hyperuricémie ».

Conclusion : Bien que la concentration sérique en acide urique (corrigée en fonction de l'âge gestationnel par l'intermédiaire d'un score Z) soit utile sur le plan clinique pour ce qui est de la prévision des issues indésirables périnatales chez les femmes hospitalisées présentant une prééclampsie, elle ne compte pas une utilité semblable en ce qui concerne les issues indésirables maternelles.

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INTRODUCTION

Despite advances in care, preeclampsia remains a leading cause of maternal and perinatal morbidity and mortality worldwide.[1] Preeclampsia affects multiple organ systems and can lead to severe renal, hepatic, neurological, and cardiopulmonary complications. Often the fetus is affected, and adverse perinatal outcomes include preterm birth, intrauterine growth restriction, and death. Ultimately, delivery is the only definitive treatment for preeclampsia; however, many cases can be managed expectantly with increased maternal and fetal monitoring, maternal blood pressure control, and maternal seizure prophylaxis. The challenge in caring for women with preeclampsia is to identify those who are at increased risk for complications so that appropriate and timely delivery can be offered. The Pre-eclampsia Integrated Estimate of RiSk research program was conceived to address this critical need in preeclampsia management. Using a combination of maternal demographics, signs, symptoms, and laboratory findings, the fullPIERS model can successfully identify women at risk for preeclampsia complications so that they can access appropriate care[2]; the miniPIERS model uses solely demographics, symptoms, and signs.[3]

A frequently reported laboratory finding in women with preeclampsia is elevated serum uric acid. Most accept that hyperuricemia in women with preeclampsia is primarily a result of a reduction in glomerular filtration rate, although others have suggested a possible role for elevated uric acid levels in the pathogenesis of preeclampsia, via endothelial dysfunction.[4–6] Reports linking elevated uric acid concentrations with adverse maternal or perinatal outcomes have described mixed results. Some investigators propose that the serum uric acid concentration is useful in predicting either adverse maternal or fetal outcomes,[7–9] while others suggest that an increased uric acid concentration is a poor predictor of maternal and fetal outcomes.[3,10,11] Part of the challenge in assessing uric acid as a marker in women with preeclampsia is that the serum uric acid concentration is known to vary throughout normal gestation.[12] To address this, Roberts et al.[9] and more recently Hawkins et al.[13] proposed using a gestational age-corrected *Z* score, based on the data of Lind et al.,[12] and concluded that measurement of serum uric acid aids in the prediction of adverse maternal and particularly perinatal outcomes.

The goal of this study was to assess, among a large cohort of 2514 women hospitalized with preeclampsia, whether the maternal serum uric acid concentration (corrected for gestational age) will identify women at increased risk for adverse maternal or perinatal outcomes.

ABBREVIATIONS

AUC	area under the curve
PIERS	Pre-eclampsia Integrated Estimate of RiSk
ROC	receiver operating characteristic

METHODS

Data for this study were obtained from PIERS, an ongoing international prospective study of women admitted to hospital with preeclampsia.[2] The following tertiary obstetric centres were involved: in Canada, British Columbia's Women's Hospital, Vancouver, BC; Kingston General Hospital, Kingston, ON; Ottawa Hospital, Ottawa, ON; and Centre Hospitalier Universitaire de Sherbrooke, Sherbrooke, QC; in the United Kingdom, St. James's University Hospital, Leeds and Nottingham University Hospital, Nottingham; in Australia, King Edward Memorial Hospital, Subiaco, Western Australia; and in New Zealand, Christchurch Women's Hospital, Christchurch. Data were collected between September 2003 and December 2011. Until 2007, four sites required subjects to provide informed consent prior to enrolment. Thereafter, women were enrolled as part of a continuous quality improvement project at all but one site. Regardless of timing, local research ethics boards approved participation at each site before subject recruitment.

The PIERS study[2] collected data on women with:

1. hypertension and proteinuria,
2. hypertension and hyperuricemia,
3. HELLP syndrome, and
4. superimposed preeclampsia.

In the current study, our primary analysis included only women with hypertension and proteinuria. Preeclampsia was defined as hypertension (systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg