Accurately Predicting the Risk of Serious Maternal Morbidity in Preterm Preeclampsia

Can It Be Done?

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The advent of antenatal care during the early 20th century and advances in obstetric management of pregnancies complicated by preeclampsia has drastically improved outcomes for women and their babies. Yet, even with advances, hypertensive disorders in pregnancy remain a leading cause of direct maternal mortality. Globally, hypertensive disorders of pregnancy are responsible for 10% to 22% of maternal deaths.[1] The developing world shoulders most of this terrible burden: a staggering 99% of all maternal deaths.[2] Preeclampsia is also a major cause of maternal morbidity.[3]

Encouragingly, aspirin use from early pregnancy can prevent preeclampsia developing, particularly early onset disease, for a significant number of women.[4] However, for those who do develop preeclampsia, progressive end-organ dysfunction is the natural course while women remain undelivered. But preeclampsia is also highly heterogeneous; some women remain undelivered for weeks with stable disease, while others deteriorate rapidly and develop severe life-threatening features. Currently, when women present with preeclampsia, clinicians have no way to predict who will remain stable and who will spiral rapidly toward life-threatening organ injury. Developing a prediction tool would be of immense use for clinicians juggling patient care and allocating precious hospital resources. In this edition of *Hypertension*, Ukah et al[5] assess the use of such a prediction tool in women with early-onset preeclampsia.

Clinical tools developed to predict adverse outcomes are widely used in other clinical specialties—for example, the APACHE II scoring system (Acute Physiology and Chronic Health Evaluation II) to estimate a patient's mortality risk on admission to an intensive care unit, the SOFA scoring system (Sequential Organ Failure Assesment) to predict the risk of mortality in the setting of sepsis, and Well's criteria for predicting those most likely to have a pulmonary embolus.[6,7] Ukah et al[5] use the fullPIERS model (Preeclampsia Integrated Estimate of Risk). Developed in 2011, the model aims to assist care providers to more accurately identify women admitted with preeclampsia at greatest risk of an adverse maternal outcome.[8] They defined a serious adverse outcome as maternal death or a serious morbidity affecting the neurological, renal, hepatic, hematological, or cardiorespiratory system. The model was developed and validated in a cohort of 2023 women admitted to tertiary care facilities in high-income countries.[8] Thirteen percent of women experienced an adverse outcome during their admission, with 40% of these occurring within the first 48 hours of admission. The model showed excellent performance with an area under the receiver operating characteristic curve of 0.88 (95% CI, 0.84–0.92).[8] The model was designed to be pragmatic and easy to use, so is rationalized to require only 6 variables. These include parameters that can be determined on history alone, such as gestational age and the presence of chest pain or dyspnea. However, other parameters in the model—maternal oxygen saturation, platelet count, creatinine, and aspartate transaminase levels—do require equipment and basic pathology services. In the study population within which the fullPIERS model was generated, 4% of women met the definition of being high risk of an adverse outcome (defined as ≥30% risk), of which 59% did in fact experience an adverse event. This compares to 65% of women stratified as low risk (<2.5% risk), of which 1% experienced a serious adverse event during their admission.[8] Overall, the fullPIERS model identified 75.5% of women as high risk who subsequently experienced an adverse event.

Pregnancies complicated by early-onset preeclampsia (occurring <34 weeks gestation) carry an increased risk of adverse maternal outcomes.[3] As such, Ukah et al[5] set out to validate the performance of the fullPIERS model among 1388 women with early-onset preeclampsia. This assessment was undertaken in 3 preexisting cohorts of women with early-onset preeclampsia from high-income countries. They confirm that the fullPIERS model shows good discriminatory performance in these combined populations with an area under the receiver operating characteristic curve of 0.80 (95% CI, 0.75–0.86),[5] a finding consistent with subgroup analysis from the original fullPIERS cohort.[8] While the model shows good performance in all populations studied, it performs most favorably when applied to populations with a high prevalence of adverse outcomes, as was seen among the Danish PETRA cohort (Preeclampsia

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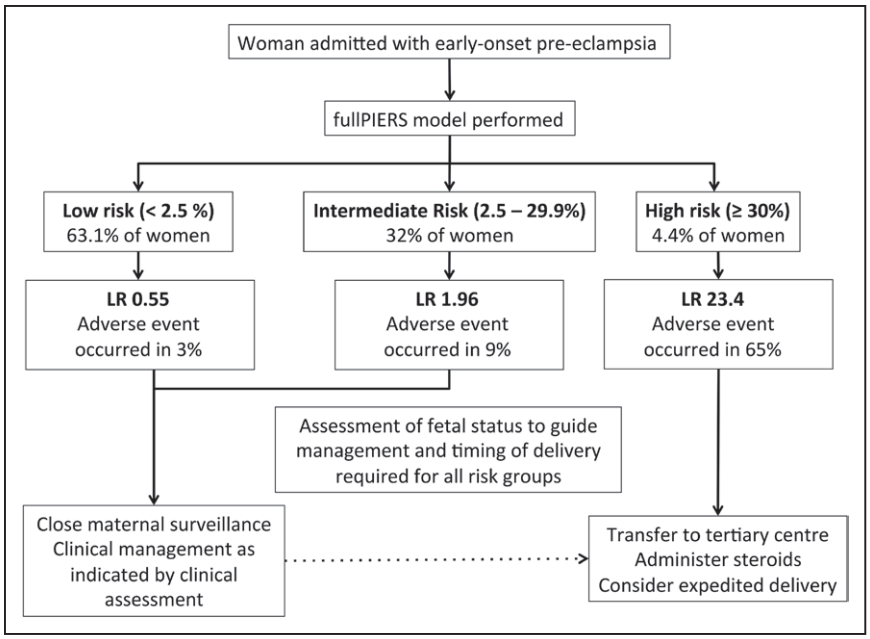

Figure. Flowchart of risk stratifications, associated likelihood ratios (LR) of an adverse event, and clinical recommendations.

Eclampsia Trial Amsterdam).[5] Overall, 16% of women had an adverse outcome during their admission, with 45% of them occurring within the first 48 hours. The Figure demonstrates the proportion of women identified as low, intermediate, or high risk of an adverse outcome, together with the likelihood ratio of an adverse outcome and the percentage of women affected within each risk group. The most common adverse events seen were the development of thrombocytopenia (platelets $<50\times10^9$/L) or placental abruption. Perhaps reflecting the more unpredictable course of early-onset disease and sometimes its rapidly progressive nature, a 3-fold increase in the rate of adverse outcomes within 48 hours of admission were seen among those stratified as low risk (<2.5% risk) compared with the original fullPIERS cohort (3% compared with 1%).

While the fullPIERS model seems to perform well in high-income countries, it also needs to be applicable in the developing world where the greatest burden of disease exists. A retrospective application of the model in a cohort of women with hypertensive disease in pregnancy from low- and middle-income countries has been undertaken. Limitations did exist in obtaining all variables for the model, likely reflecting the challenges and limitations in accessing these resources in an under-resourced setting. Furthermore, the model performed only modestly as a rule-in test (likelihood ratio, 5.9; 95% CI, 4.23–8.35) for women at highest risk of an adverse event.[9] Alternative models, such as miniPIERS,[10] may prove more useful in a low-resource setting, but neither model has been assessed in early-onset preeclampsia within low- and middle-income countries.

The question remains as to how clinicians at the coalface can integrate this model. Ukah et al[5] propose that women identified as high risk should be delivered immediately in centers that are equipped to care for mothers and babies at these premature gestations. Given there are definite false positives when applying this model, we are not so sure. The fullPIERS model has been developed as a prediction tool for maternal adverse outcomes using population data, while clinicians need to constantly balance the risk–benefit ratio for individual mothers and babies. Given the serious implications arising from inflicting significant prematurity when iatrogenically ending a pregnancy affected by early-onset preeclampsia, the impact of false positives are not at all trivial. Thus, caution needs to be exercised in initiating iatrogenic preterm delivery based on fullPIERS risk stratification alone.

However, we think an important clinical role for the model exists in high-income countries, where it has been well validated by the team. Given evidence to guide management is rarely black and white, clinicians are masters at considering all the evidence at hand and making a clinical judgment. And the information before them can be complex—from the resources available to them, buying time for corticosteroids to take effect, to the expectations of the family. While we are unsure whether a risk score generated by the fullPIERS algorithm should be the overriding factor in clinical decision-making, it could be a powerful adjunct tool to help guide clinicians (see Figure). Just like APACHE II, SOFA, and Well's. In some cases where there is true indecision among clinicians whether or not to deliver the preterm preeclamptic patient, the tool could be used to break that equipoise. Alternately, a patient stratified as high risk but in a facility replete with full obstetric and neonatal facilities, delivery could still be delayed in the interest of gestational advancement, but the patient watched like a hawk for signs of deterioration.

Disclosures

None.

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