Predicting pre-eclampsia

A challenge that shouldn’t distract us from improving antenatal care across the board

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A healthy mother and baby are the desired outcomes of all antenatal care, yet WHO estimates that every year around the world there are about 303 000 maternal deaths, 2.6 million stillbirths, and 2.7 million neonatal deaths. Pregnancy and birth are transformative life events, but optimal preparation for transition to motherhood often receives little attention. Pregnancy in itself is not an illness or a disease, but comorbidities or evolving complications can lead to mortality or serious morbidity. Risk stratification of pregnant women has been proposed to enable increased surveillance and appropriate prophylactic interventions for those at greater risk of complications, while normalising healthy women who have a high likelihood of uncomplicated pregnancy. The linked study by Macdonald-Wallis and colleagues (doi:10.1136/bmj.h5948) reports the development and validation of a new prediction model for pre-eclampsia. They concluded that incorporating routinely collected blood pressure measurements into models based on early pregnancy maternal characteristics would improve risk stratification, “facilitating a reduction in scheduled antenatal care” for those at low risk of pre-eclampsia.

The current schedule for antenatal care in many high income countries has a scant evidence base and focuses on one aspect of medical input without necessarily considering the holistic needs of the woman and her emergent family. Pre-eclampsia is associated with a range of complications, including maternal cerebrovascular events, hepatic and renal impairment, and pulmonary oedema, any of which might be life threatening; it is also associated with fetal growth restriction with attendant increased risks of stillbirth and neonatal death in all settings. For many years, hypertensive disorders of pregnancy have been responsible for a substantial proportion of maternal deaths in high and low income countries, alongside other causes such as postpartum haemorrhage and deaths secondary to cardiac or psychiatric comorbidities. Thus it remains an important goal to predict and prevent pre-eclampsia to reduce avoidable morbidity and mortality in both mother and baby, but we must not ignore prediction and prevention of other adverse maternal and perinatal outcomes, and the promotion of health and wellbeing, if we are to achieve and exceed the millennium development goals to improve maternal health and reduce child mortality.

Around 70 risk prediction models have been reported for pre-eclampsia, but few undergo external validation and none has been tested against clinical judgment or routinely introduced into widespread clinical practice. These latter issues are not unique to this specialty; in the few cases where models have been tested against clinical judgment they were rarely superior. Decreased antenatal monitoring (potentially difficult as many “low risk” women are in second pregnancies and therefore already on a reduced schedule) might not be enough to drive implementation of a prediction model for pre-eclampsia. Prophylactic low dose aspirin, associated with a 17% reduction in pre-eclampsia and 14% decrease in perinatal death, is already recommended for women with known risk factors for pre-eclampsia.

In the linked study, the proposed model formalises some of the process that clinicians currently adopt informally at sequential antenatal visits—that is, adapting their perception of ongoing risk by incorporation of new information on blood pressure. The model showed good test performance for ruling out disease; for a fixed detection rate of 95% of cases, however, the positive predictive value of the basic and enhanced model was low at 4-5%, a minimal increment on the pre-test incidence (2.9%) in the population. As this model was developed and validated in largely white European cohorts with mainly normal body mass index, test performance in a more diverse population could lead to reduced predictive values.

The proposed benefit therefore comes from downsizing visits for the 30% of women who are judged by the model to be low risk, but this would reduce the broader spectrum of antenatal interactions that occur at each visit, not just those related to pre-eclampsia. A Cochrane review on alternative packages of antenatal care for low risk pregnant women found some evidence from trials in low and middle income countries that reduced visits might be associated with increased perinatal mortality;
women in all settings were less satisfied with the reduced schedule of visits, and for some women the gap between visits was perceived as too long.

Alternatively, if the main purpose of the antenatal visit is solely to obtain a blood pressure reading to exclude development of pre-eclampsia, then the introduction of self monitoring of blood pressure, empowering women to manage their own health, might be more valuable. At present, we have insufficient data on the validity or reliability of self monitoring in pregnancy, but it has considerable potential.

Development of a high performance prediction model for pre-eclampsia is challenging because pre-eclampsia is so heterogeneous clinically. Expecting one test or model to predict a condition that varies from severe early onset disease with fetal growth restriction and a clear placental phenotype, to onset at term in a mother with an appropriately grown fetus and predominantly maternal complications remains problematic, even before comparison with clinical judgment. Antenatal care, however, is about much more than obtaining two numbers representing systolic and diastolic blood pressure. We should re-examine much more holistically whether current schedules of antenatal care are fit for purpose and give women everywhere the best possible chance of a healthy pregnancy, a complication free delivery, and a healthy baby.

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11 Roberts JM, Bell MJ. If we know so much about pre-eclampsia, why haven’t we cured the disease? J Reprod Immunol 2013;99:1-9.