

# Introduction

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Hypertensive disorders complicate 5–10% of pregnancies worldwide, with limited data suggesting an upward trend in incidence most likely related to increasing maternal weight and sedentary lifestyle (Chapter 4). With few differences, all international societies define the hypertensive disorders of pregnancy as chronic hypertension, gestational hypertension and pre-eclampsia (Chapter 3). Although women with pre-eclampsia have the greatest risk of maternal and perinatal complications, what constitutes pre-eclampsia is controversial, and diagnostic distinctions are often blurred. As such, it is important to view all women with a hypertensive disorder of pregnancy and their babies as being at increased risk of mortality and morbidity, and act accordingly.

Pre-eclampsia remains one of the top five causes of maternal and perinatal mortality worldwide. Our best estimate is that pre-eclampsia claims the lives of more than 70,000 women per year and more than 500,000 of their fetuses and newborns; this is equivalent to the loss of 1600 lives per day<sup>1</sup>. More than 99% of these losses occur in low- and middle-income countries (LMICs), particularly those on the Indian subcontinent and sub-Saharan Africa<sup>2</sup>. For every woman who dies, it is estimated that another 20 suffer a life-altering morbidity<sup>3,4</sup>.

Given that maternal (and perinatal) deaths and sequelae result primarily from delays in triage, transport and treatment, it would seem important for the global community to turn its attention to community-based care<sup>1</sup>. A community-focused approach could include community engagement and use of innovative technologies, like smartphone applications could be used to support community-based health workers. In addition, however, care at facility must be of high quality in order for outcomes to be improved, a point that has been highlighted by the move towards encouraging more facility births and concerns about the quality of care received there. In the World Health Organization Multicountry Survey on Maternal

and Newborn Health (WHOMCS) that covered 357 health facilities in 29 countries, high coverage of essential interventions was not associated with reduced maternal mortality<sup>5</sup>. As such, attention must also be focused on strengthening provision of evidence-based comprehensive emergency obstetric care (CEmOC)<sup>6</sup>, conducting maternal death and near-miss morbidity surveillance and response ([www.who.int/mdsr](http://www.who.int/mdsr)), and performing large-scale effectiveness evaluations, with the district as the unit of design and analysis and the clear message that there is local ownership, by women, communities, care providers and government<sup>7</sup>.

Knowledge is power, and the impact that evidence-based knowledge can have on practice and policy is highlighted by the WHO IMPAC (Integrated Management of Pregnancy and Childbirth) guidance documents (2000) ([www.who.int/preadolescence/topics/maternal/impac/en/](http://www.who.int/preadolescence/topics/maternal/impac/en/)). These were among the first WHO documents to recommend MgSO<sub>4</sub> for eclampsia prevention and treatment. The information was adopted in national guidelines in many African and Asian countries, and formed the core of EmOC training packages, as well as led to policy changes in countries on use of MgSO<sub>4</sub> as reflected in national medicines lists.

In the 1980s, it was noted that the dramatic decline in maternal mortality over the prior 50 years in Britain was related to the standard of maternity care, even in the face of ongoing social deprivation:

“In obstetrics the difference between a careful doctor (or midwife) and a careless one can be very large indeed. The introduction, therefore, of an ordinary standard of good obstetric practice, not necessarily at the level of the hospital specialist, can be expected to have a profoundly beneficial effect in societies that still suffer high maternal mortality.”

Irvine Loudon, *British Med J* 1986<sup>8</sup>

The purpose of this book is to promote evidence-based maternity care for all women, regardless of where they live. This text covers all clinical aspects of hypertensive disorder of pregnancy diagnosis and management of women in both well- and under-resourced settings. Each chapter begins with a synopsis of the material, followed by a summary of the evidence. Best practice points are designed to provide practical advice; the evidence on which the recommendations are based, and the strength of each recommendation, is presented in appendix tables for readers interested in more detail. There is specific discussion of priorities for under-resourced settings, what international guidelines say, and logical future directions. Each chapter includes material in the appendices, ranging from the evidence grading for recommendations (mentioned above) to internal guideline recommendations and policy brief templates (e.g., Chapters 1 and 2) and practice drills (Chapter 8).

Chapters 1 and 2 address the diagnosis of hypertension and proteinuria, the two most common diagnostic criteria for pre-eclampsia and the only ones for which there is international agreement.

The diagnosis of hypertension is based on systolic and diastolic blood pressure values, taken in any setting by auscultatory or oscillometric (automated) devices. In LMICs, the assessment of service gaps and programmatic responses to ensure access to blood pressure measurement are a priority, supported where appropriate by implementation research.

Increasingly, it is recognised that proteinuria is not essential for the diagnosis of pre-eclampsia, which can be based on other end-organ complications (such as elevated liver enzymes). Although heavy proteinuria has been linked with an increased risk of stillbirth in a 'signs and symptoms only' model of maternal risk (i.e., miniPIERS), we lack the ability to identify a level of proteinuria above which maternal and/or perinatal risk is heightened. Therefore, at present, we rely on the detection of proteinuria that exceeds what is normally excreted by healthy pregnant women. Proteinuria detection methods are also a matter of keen debate, with all available methods having advantages and disadvantages.

Chapter 3 presents the classification of the hypertensive disorders of pregnancy, relating

categories directly to maternal and perinatal complications and recommendations for surveillance. In addition to the universal categories of pre-existing (chronic) hypertension, gestational hypertension and pre-eclampsia, other categories of white coat and masked hypertension are also discussed. Of note, there is tremendous controversy over whether the term 'severe' pre-eclampsia should be used and, if so, how it should be defined. We endorse the 2014 Canadian approach of defining 'severe' pre-eclampsia according to the presence of severe complications that mandate delivery so timing of delivery is clear to those with less experience with the disease<sup>9</sup>.

The distinction between identification of women at increased risk of pre-eclampsia (Chapter 5) and the identification of women at increased risk of complications once a hypertensive disorder of pregnancy has been diagnosed (Chapter 3) is an important one. The potential for accurate prediction of pre-eclampsia lies in multivariable models, with the most promising predictors being the angiogenic factors and uterine artery Doppler velocimetry combined with other biochemical factors. There is an urgent need to evaluate how new diagnostic and risk-stratifying biomarkers can be incorporated into existing protocols and to improve both prediction of pre-eclampsia itself among women who are well, as well as the prediction of complications among women who already have pre-eclampsia. Having these biomarkers available as point-of-care tests in all clinical settings would be the ultimate goal.

Preventative strategies for pre-eclampsia and its complications are based on risk (Chapter 6). Women are classified as being at 'low' or 'increased' risk of pre-eclampsia most commonly by the presence or absence of one or more of the risk markers discussed in Chapter 5. There is strong evidence that low risk women who have low dietary intake of calcium (<600 mg/d) may benefit from calcium supplementation (of at least 1 g/d, orally) to prevent pre-eclampsia. High risk women are recommended to take calcium supplementation (of at least 1 g/d) if calcium intake is low, and are also recommended to initiate low-dose aspirin (75–100 mg/d) at bedtime before 16 weeks' gestation, when most of the physiologic transformation of uterine spiral arteries occurs, or even before pregnancy; such early intervention has the greatest potential to decrease the early forms of

pre-eclampsia that are associated with incomplete transformation of uterine spiral arteries. Widespread implementation of these interventions is recommended to help prevent pre-eclampsia and its complications.

The management of hypertensive disorders of pregnancy involves non-pharmacological (Chapter 7) as well as drug, blood product and fluid administration (Chapter 8).

Although widespread, use of lifestyle (e.g., stress reduction, increased rest at home, or bed rest) to manage women with pre-eclampsia is based on a lack of high quality evidence, as are dietary interventions (e.g., salt reduction). There is also little information about the relative benefits and risks of place of care if delivery is deferred. In under-resourced settings, addressing a lack of safe and available transport from community to facility has enormous potential to address maternal and perinatal mortality and morbidity. Also, communities have a critical role to play in ensuring that women and their families are prepared for birth and any complications that may arise, from the hypertensive disorders of pregnancy or other conditions that may arise.

Women with pre-existing or gestational hypertension are at risk of any of the hypertensive disorders of pregnancy evolving into pre-eclampsia, a multisystem disorder of endothelial dysfunction. As such, attention must be paid to judicious fluid management, antihypertensive therapy of severe and non-severe hypertension with oral or parenteral agents, magnesium sulphate ( $MgSO_4$ ) for eclampsia prevention and treatment as well as fetal neuroprotection with birth at <34 weeks, antenatal corticosteroids for acceleration of fetal pulmonary maturity, and various therapies for HELLP syndrome (haemolysis, elevated liver enzyme, low platelet), including transfusion of blood products and, possibly, corticosteroids. The WHO Model List of Essential Medicines includes all of the aforementioned interventions other than fluid therapy for pregnant women. We must advocate for use of effective interventions whether we practice in well- or under-resourced settings.

The phrase, “planned childbirth on the best day in the best way,” alludes to the fact that there is a myriad of considerations regarding timing (and mode of) childbirth in women with a hypertensive disorder of pregnancy, particularly pre-eclampsia (Chapter 9). Complicating this decision-making is

inaccurate determination of gestational age, difficulty identifying those women who are at particular risk of an adverse outcome if pregnancy is prolonged, and the fact that ‘severe’ pre-eclampsia has been variably defined by international organisations and, yet, all list ‘severe’ pre-eclampsia as an indication for delivery. Regardless, the past decade has seen publication of a significant body of work that informs our decisions about timing of delivery in women with a hypertensive disorder of pregnancy, particularly pre-eclampsia. Childbirth is recommended for women with pre-eclampsia or gestational hypertension at term for maternal benefit, although expectant care is recommended for women with any hypertensive disorder of pregnancy at late preterm gestational ages to reduce neonatal respiratory morbidity (associated with labour induction and Caesarean delivery). Small trials suggest that expectant care of women with pre-eclampsia from fetal viability to 33<sup>+6</sup> weeks reduces neonatal morbidity, but the magnitude of maternal risk has not been fully quantified. There are no trials to inform timing of delivery determination of women with chronic hypertension, but observational literature suggests that the optimal period is between 38<sup>+0</sup> and 39<sup>+6</sup> weeks.

Mode of delivery is usually determined by usual obstetric indications (Chapter 9). However, if there is evidence of fetal compromise at a gestational age remote from term, women with a hypertensive disorder of pregnancy may benefit from delivery by Caesarean. It is particularly important for women with a hypertensive disorder of pregnancy to have the third stage of labour actively managed, particularly in the presence of thrombocytopenia or coagulopathy. Ergometrine maleate should not be administered to women with any hypertensive disorder of pregnancy given its potential to precipitate severe hypertension.

No text on a common and dangerous pregnancy-related complication would be complete without discussion of the anaesthetic issues. Chapter 10 presents a focused discussion of anaesthetic issues specifically related to parturients with a hypertensive disorder of pregnancy. Early consultation and involvement of anaesthesia will result in the best possible outcome for these women and their babies. Provision of effective analgesia for labour will not only decrease pain, but also attenuate its effects on blood pressure and cardiac output. In addition,

epidural analgesia benefits the fetus by decreasing maternal respiratory alkalosis, compensatory metabolic acidosis and release of catecholamines. An effective labour epidural can be used should a Caesarean delivery be required, avoiding the need for general anaesthesia. Both neuraxial (epidural, spinal, continuous spinal and combined spinal epidural) and general anaesthesia are appropriate for Caesarean delivery. The choice of technique will depend on the overall condition of the parturient, the urgency of the situation, and whether there are contraindications to any particular technique. Challenges associated with anaesthesia include maintaining haemodynamic stability during laryngoscopy and intubation with general anaesthesia, or after sympathetic block secondary to neuraxial anaesthesia. Although neuraxial anaesthesia is preferred to general anaesthesia, owing to potential problems with the airway in the woman with pre-eclampsia, neuraxial anaesthesia may not be possible in the presence of a low platelet count or other coagulation abnormality. The interaction of non-depolarising muscle relaxants (as part of general anaesthesia) and  $MgSO_4$  will limit their use in the woman with pre-eclampsia. Adequate analgesia and ongoing monitoring are important components of overall postpartum management.

Chapter 11 emphasises the importance of postpartum care, to prevent short-term complications, as well as initiating thoughts about the implications for future pregnancy and long-term health in an evolving circle of life (below). In the immediate postpartum period, hypertension may worsen transiently, especially between days 3 and 6 when blood pressure peaks. Hypertension and pre-eclampsia may even develop for the first time postpartum. Hypertension, proteinuria and the biochemical changes of pre-eclampsia begin to

resolve by 6 weeks postpartum but may persist for longer, especially when those changes have been extreme (e.g., nephrotic-range proteinuria). Care in the 6 weeks postpartum includes management of hypertension, ensuring resolution of biochemical changes, and screening for secondary causes of hypertension in women with resistant hypertension, impaired renal function, or abnormal urinalysis. Care providers must be aware of the mental health implications of the hypertensive disorders of pregnancy, such as anxiety, depression and post-traumatic stress disorder. The hypertensive disorders of pregnancy are also associated with a number of long-term complications and the postpartum period provides an ideal window of opportunity to address these risks, such as premature cardiovascular disease and chronic kidney disease. Women with a history of a hypertensive disorder of pregnancy should adopt a heart-healthy lifestyle and should be screened and treated for traditional cardiovascular risk factors according to locally accepted guidelines.

It is hoped that this text will play a role in promoting high-quality, evidence-based care of women with the hypertensive disorders of pregnancy, because none should die or become seriously ill owing to their own ignorance or that of their care providers.

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