Preeclampsia in Low and Middle Income Countries—Health Services Lessons Learned From the PRE-EMPT (PRE-Eclampsia–Eclampsia Monitoring, Prevention & Treatment) Project

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Abstract

The hypertensive disorders of pregnancy, in particular preeclampsia, matter because adverse events occur in women with preeclampsia and, to a lesser extent, in women with the other hypertensive disorders. These adverse events are maternal, perinatal, and neonatal and can alter the life trajectory of each individual, should that life not be ended by complications. In this review we discuss a number of priorities and dilemmas that we perceive to be facing health services in low and middle income countries as they try to prioritize interventions to reduce the health burden related to preeclampsia. These priorities and dilemmas relate to calcium for preeclampsia prevention, risk stratification, antihypertensive and magnesium sulphate therapy, and mobile health. Significant progress has been and is being made to reduce the impact of preeclampsia in low and middle income countries, but it remains a priority focus as we attempt to achieve Millennium Development Goal 5.

Résumé

Les troubles hypertensifs de la grossesse, particulièrement la prééclampsie, ont de l'importance puisque des événements indésirables se manifestent chez des femmes présentant une prééclampsie et, dans une moindre mesure, chez des femmes présentant d'autres troubles hypertensifs. Ces événements indésirables sont de nature maternelle, périnatale et néonatale, et peuvent modifier la vie des personnes qui les connaissent, lorsque celles-ci survivent aux complications. Dans cette analyse, nous discutons d'un nombre de priorités et de dilemmes auxquels doivent faire face les services de santé des pays à revenu faible ou moyen au moment de tenter de hiérarchiser les interventions en vue d'atténuer le fardeau de santé lié à la prééclampsie. Ces priorités et ces dilemmes sont liés à l'administration de calcium aux fins de la prévention de la prééclampsie, à la stratification du risque, aux traitements aux antihypertenseurs et au sulfate de magnésium, et à la santé « mobile ». Bien que des progrès significatifs aient été réalisés et continuent d'être réalisés en vue d'atténuer les effets de la prééclampsie au sein des pays à revenu faible ou moyen, cette problématique demeure une priorité dans le cadre de nos tentatives d'atteindre l'objectif 5 du Millénaire pour le développement.

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BACKGROUND

Preeclampsia, although commonly defined by the presence of both significant hypertension and heavy proteinuria, is a pregnancy- and placenta-specific form of systemic inflammation with multiple target organs (Figure).[1] As far as we can determine, preeclampsia and eclampsia claim the lives of approximately 72 000 women and 500 000 fetuses and newborns each year—a loss of almost 1600 lives per day.[2] Over 99% of these losses occur in low and middle income countries, particularly in sub-Saharan Africa and on the Indian subcontinent.[2] In the Americas, preeclampsia and eclampsia are the leading cause of direct maternal mortality.[3–5]

Currently, the singular way to initiate resolution of the maternal syndrome of preeclampsia is to deliver the placenta.[1] However, the maternal syndrome of preeclampsia may present de novo postpartum and, especially with early-onset preeclampsia, cause transient postpartum deterioration.[1] Therefore, even timely delivery does not necessarily avoid all end-organ complications of the disorder. In addition, the life-altering and life-threatening complications (e.g., stroke, acute renal failure, eclampsia, pulmonary edema, and placental abruption) probably increase the significant health burden of preeclampsia by at least five-fold.[6,7]

As a group, we believe that the global community (clinicians, researchers, policy makers, governments, health authorities, and other stakeholders) should focus efforts on reducing the excess number of adverse maternal and perinatal events in women whose pregnancies are complicated by preeclampsia, rather than focus solely on the surrogate of these risks, the diagnosis of preeclampsia.

Given that preeclampsia-related maternal and perinatal deaths and permanent sequelae result primarily from delays in diagnosis, triage, transport, and treatment,[2] an important direction for new initiatives related to improving preeclampsia-related outcomes may be to enhance the availability of life-saving interventions in the communities in which vulnerable women reside. Such interventions may vary from improving the status of pregnant women and facilitating timely decision-making when complications arise, to initiating life-saving therapies (e.g., magnesium sulphate and antihypertensive agents) prior to urgent transfer to an effective and adequately resourced emergency obstetric care facility.

In 2011, the University of British Columbia was awarded the four-year PRE-eclampsia–Eclampsia Monitoring, Prevention & Treatment project grant by the Bill & Melinda Gates Foundation. The overarching theme of this proposal is "reducing the maternal and perinatal consequences of preeclampsia." Through this grant we aim to determine the impact of this program of research on those outcomes.

The primary objectives of PRE-EMPT are three community-level and primary health centre-level intervention studies tailored to LMIC settings and related to prevention, monitoring, and treatment. The secondary objectives are

1. developing a multifaceted international research collaboration, and
2. LMIC-oriented preeclampsia knowledge translation activities.

We describe here examples of what we have learned to date from these objectives, and the implications derived from our current position for health service decision-making, especially in resource-challenged settings.

ABBREVIATIONS

AUC ROC	area under the receiver-operator characteristic curve
BP	blood pressure
EPIC	European Prospective Investigation into Cancer and Nutrition study
HR	hazard ratio
LMIC	low and middle income countries
MDG	Millennium Development Goal
PIERS	Pre-eclampsia Integrated Estimate of RiSk
PRE-EMPT	Pre-eclampsia–Eclampsia Monitoring, Prevention & Treatment
RDA	recommended daily allowance
RR	relative risk

PREVENTION

Calcium Supplementation to Reduce the Incidence of Preeclampsia: Should We Provide This to High-Risk Women? If Yes, at What Dose?

In general, preeclampsia is considerably more prevalent in low and middle income communities than in affluent communities.[8] Two striking exceptions have been identified in Ethiopia and in the Mayan Indians of Guatemala, where diets contain high levels of calcium.[9,10] Subsequent epidemiological, clinical, and laboratory studies linking preeclampsia to calcium deficiency have been outlined in a recent systematic review of calcium supplementation during pregnancy.[11] The conclusion of this systematic review, and that of a parallel meta-analysis,[12] was that supplemental calcium (at least 1 g daily) from mid-pregnancy is associated with a modest reduction in rates of preeclampsia, and a more notable reduction in its severe manifestations, particularly among women at increased risk or with low dietary calcium intake. However, we have found no report of randomized controlled trials of calcium supplementation commenced before pregnancy.