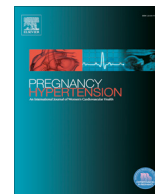




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Hypertensive disease in pregnancy in Botswana: Prevalence and impact on perinatal outcomes

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ABSTRACT

Objectives: Perinatal morbidity in sub-Saharan Africa has been attributed to infection, obstetric emergencies, and preterm birth, but less is known about hypertension in pregnancy. Our objective was to characterize the prevalence of hypertension in pregnancy and the impact of hypertension on perinatal outcomes in sub-Saharan Africa.

Study design: We performed surveillance of obstetric records at eight of the largest public hospitals in Botswana. Women were included in this analysis if they were HIV-uninfected and had singleton gestations and at least one prenatal blood pressure measurement.

Main outcome measures: We measured stillbirth, preterm birth, small for gestational age, and neonatal death in women with and without hypertension in pregnancy.

Results: We included 14,170 pregnancies. Hypertension occurred in 3156 (22.2%) women, with 602 (19.1%) defined as severe. Severe hypertension increased risk of stillbirth (RR 4.4; 95% CI 3.2–6.2), preterm birth (RR 2.5; 95% CI 2.2–2.8), small for gestational age (RR 2.7; 95% CI 2.3–3.1) and neonatal death (RR 5.1; 95% CI 2.9–5.6). Non-severe hypertension increased risk of stillbirth (RR 2.0; 95% CI 1.5–2.7), preterm birth (RR 1.2; 95% CI 1.1–1.3), and small for gestational age (RR 1.6; 95% CI 1.4–1.8). Perinatal outcomes were worse in women with hypertension who had spontaneous preterm birth compared to those who underwent iatrogenic preterm delivery.

Conclusions: Hypertension in pregnancy is common in Botswana and leads to a large number of adverse outcomes. Improved management of hypertension in pregnancy may improve perinatal morbidity and mortality.

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1. Introduction

Hypertensive disease in pregnancy significantly impacts maternal and perinatal outcomes worldwide, particularly in low and middle income countries (LMIC) [1]. A majority of adverse perinatal outcomes in LMICs are thought to be due to non-hypertensive etiologies, including infection [2–4], obstructed labor [5,6], and preterm or postterm pregnancy [3,7]. However, approximately one quarter of perinatal deaths are attributed to preeclampsia or eclampsia in LMICs [8] and infants born to mothers with

preeclampsia have a threefold higher rate of perinatal mortality in low income countries than in high income countries [1]. This disparity is likely due to limitations in neonatal care for preterm infants and limited access to emergency obstetric services and close fetal monitoring to prevent stillbirth [6,9].

While eclampsia and preeclampsia have been identified as major causes of perinatal mortality worldwide, they are relatively uncommon, affecting approximately 4% of pregnant women in sub-Saharan Africa [10]. In contrast, non-preeclamptic hypertension is far less studied in LMICs, especially in sub-Saharan Africa where the attributable risk of chronic hypertension on stillbirth is highest [3]. Given that non-preeclamptic hypertension is far more common [11], may be difficult to identify and manage without strong primary health systems [12] and may have a large

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overall impact on perinatal outcomes [2,13], a better overall understanding of its impact on perinatal outcomes is needed in a region that ranks highest in perinatal mortality (28 deaths per 1000 births) [14].

Botswana represents a unique setting to study hypertension in pregnancy, as 99% of women deliver in an institutional setting [15], the majority of women receive antenatal care [2], and anti-hypertensive medications are widely available [16]. In this study, we document the prevalence of hypertensive disease in a nationally representative sample of pregnancies among HIV-uninfected women in Botswana and describe the impact of hypertensive disease on perinatal outcomes.

2. Methods

We performed prospective surveillance of obstetric records at eight of the largest public hospitals in Botswana: Princess Marina Hospital in Gaborone, Nyangabgwe Hospital in Francistown, Maun General Hospital in Maun, Sekgoma Memorial Hospital in Serowe, Scottish Livingstone Hospital in Molepolole, Selebi-Phikwe Government Hospital in Selebi-Phikwe, Mahalapwe Hospital in Mahalapye, and Ghanzi Primary Hospital in Ghanzi. All women who delivered at these hospitals during the surveillance period were included in this analysis if they were HIV-uninfected, had singleton gestations, and had at least one antenatal visit with a blood pressure (BP) measurement. Women who presented in pregnancy with a history of hypertension, but who did not develop elevated blood pressure during that pregnancy, were excluded from the analysis to avoid misclassification of women with chronic hypertension as normotensive. We restricted our analysis to HIV-uninfected women to allow a targeted investigation of hypertension, as prior studies in Botswana have suggested potential confounding of the relationship between hypertension and perinatal outcomes by maternal immune status and possibly antiretroviral therapy [2,17,18].

Standard maternal demographic and medical information was abstracted from the maternal obstetric record at the time of discharge from the postpartum ward. We defined booking weight as the first weight recorded in the antenatal record. We used booking weight greater than 90 kg to approximate obesity. While pre-pregnancy body mass index would be more accurate, data on pre-pregnancy weight and height was unavailable for most women and prior studies have shown an association between booking weight itself and adverse perinatal outcomes [19]. Weight gain during pregnancy, defined as the last weight in the antenatal record minus the first weight in the antenatal record, was considered high if greater than 20 kg. Factors relating to healthcare delivery, including gestational age at first antenatal care visit, number of antenatal care visits, hospital of delivery, and maternal history of preterm birth or stillbirth also were collected. Gestational age recorded by the delivering midwife was used for all analyses, and was most often based on the patient's last menstrual period. We defined hypertension as at least one systolic BP (SBP) ≥ 140 or diastolic BP (DBP) ≥ 90 and severe hypertension as SBP ≥ 160 or DBP ≥ 110 during pregnancy. Women were considered to have chronic hypertension if they had a reported history of chronic hypertension, presented to antenatal care on anti-hypertensive medication, or developed hypertension before 20 weeks of gestation.

We assessed the risk of hypertension on the incidence of stillbirth (Apgar of 0 at 1, 5, and 10 min), preterm birth (<37 weeks of gestation), small for gestational age (SGA) (<10th percentile of weight for gestational age based on standard World Health Organization (WHO) curves), admission to the neonatal unit, and neonatal death (in-hospital death within 28 days of life). Neonatal units

in Botswana often are equipped with incubators, but rarely have ventilators or one-on-one nursing care. While not neonatal intensive care units, admission to these units represents an escalation of care. Preterm birth was defined as iatrogenic if the labor was induced or if the birth occurred by way of a planned cesarean section. Descriptive data are presented as proportion or median (interquartile range), due to a non-normal distribution. Categorical data were compared using the chi-square test, and continuous variables were compared using the Wilcoxon signed-rank test. Modified Poisson regression was used to calculate risk ratios (RR) and 95% confidence intervals (CI) [20]. We adjusted for factors that have previously been identified as confounders in the published literature.

Approval for this study was obtained from the Human Research Development Council in Botswana and the Harvard T.H. Chan School of Public Health institutional review board in Boston.

2.1. Role of the funding source

The study sponsor did not have any role in the study design, analysis or interpretation of data, the writing of the report, or the decision to submit the paper for publication.

3. Results

From August 2014 through July 2015, 14,305 HIV-uninfected women registered for antenatal care and delivered a singleton infant at one of the 8 sites included in this study, representing approximately 44% of all deliveries in Botswana to HIV-uninfected women receiving antenatal care [14]. We excluded 135 women who had a history of any type of hypertension but did not develop hypertension during the current pregnancy; thus, the included population was 14,170 women. The median maternal age at delivery was 25 (21.0–30.0) and the median number of antenatal care visits was 10 (7.0–12.0) (Table 1). The majority of women were citizens of Botswana, unmarried, non-smokers, and gained more than 20 kg during pregnancy (Table 1). Women with hypertension were slightly older, and more likely to be married, multiparous, and obese than normotensive women (Table 1). While the proportion of women with a history of stillbirth and preterm birth was overall low, a higher proportion of women with hypertension compared with normotensive women had a history of stillbirth or preterm birth.

3.1. Prevalence of hypertension in pregnancy

Overall, 3156 (22.2%) women had hypertension during pregnancy; the majority ($n = 2477$, 78.5%) developed hypertension after 20 weeks of gestation, while the remaining 21.5% ($n = 679$) had chronic hypertension. Among women with hypertension, 602 (19.1%) had severe hypertension; the majority ($n = 505$, 83.9%) of these women had chronic hypertension. Data on urine protein were only collected for 10% of women with hypertension, limiting our ability to assess for preeclampsia.

3.2. Incidence of adverse perinatal outcomes

Overall, 2294 (16.2%) babies were born preterm, 1510 (10.7%) were SGA, 281 (2.0%) were stillborn, and 136 (1.0%) died in the first 28 days. Women with severe hypertension experienced the highest incidence of poor perinatal outcomes, though women with non-severe hypertension also experienced a higher incidence of adverse perinatal outcomes than normotensive women (Fig. 1).

After adjusting for maternal age, marital status, salaried employment, and obesity, women with any hypertension were

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