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Early warning system hypertension thresholds to predict adverse outcomes in pre-eclampsia: A prospective cohort study

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ABSTRACT

Objectives: To evaluate the association between blood pressure (BP) measurements and adverse outcomes in women with pre-eclampsia.

Study design: A prospective cohort study of women with pre-eclampsia admitted to three South African tertiary facilities. BP was measured using the CRADLE Vital Signs Alert (VSA), incorporated with a traffic light early warning system; green: systolic BP < 140 mmHg and diastolic BP < 90 mmHg, yellow: systolic BP 140–159 and/or diastolic BP 90–109 mmHg (but neither is above the upper threshold), red: systolic BP ≥160 mmHg and/or diastolic BP ≥110 mmHg.

Main outcome measures: Maternal: death, eclampsia, stroke, kidney injury; process measures: magnesium sulfate use, Critical Care Unit (CCU) admission; perinatal: stillbirth, neonatal death, preterm delivery.

Results: Of 1547 women with pre-eclampsia (including 42 twin pregnancies), 33.0% of women triggered a red light on admission and 78.6% at their highest BP. Severe hypertension and adverse outcomes were common across yellow and red categories. Comparing admission red to yellow lights, there was a significant increase in kidney injury (OR 1.74, CI 1.31–2.33, trend test p = .003), magnesium sulfate use (OR 3.40, CI 2.24–5.18, p < .001) and CCU admission (OR 1.50, CI 1.18–1.91, p < .001), but not for maternal death, eclampsia, extended perinatal death or preterm delivery.

Conclusion: The CRADLE VSA, with integrated traffic light early warning system, can identify women who are hypertensive, at increased risk of severe pre-eclampsia complications and in need of escalation of care. Women who triggered a red light were at increased risk of kidney injury, magnesium sulfate use and CCU admission.

1. Introduction

Pre-eclampsia affects 3–5% of pregnancies and is a leading cause of maternal and perinatal mortality and severe morbidity globally [1,2]. In high-income countries, maternal mortality from pre-eclampsia is now rare; this is a result of prompt action following diagnosis facilitated by blood pressure (BP) and urinary dipstick proteinuria measurement [3]. In low- and middle-income countries (LMIC) settings, where 99% of all maternal deaths occur, healthcare providers often do not have access to the necessary equipment, the training to use the equipment and respond appropriately to abnormal vital signs, nor access to effective referral pathways [4]. It is in LMICs that women are dying from preventable complications of pre-eclampsia.

The CRADLE Vital Signs Alert (VSA) is a hand-held, upper-arm, semi-automated device measuring BP and pulse to facilitate prompt recognition of abnormalities in vital signs. It has been designed specifically for healthcare providers from LMICs and meets the World Health Organisation's requirements for use in low-resource settings [5]. Device accuracy has been validated for use in pregnancy, including pre-eclampsia and low BP in pregnancy [6–8]. The device incorporates a traffic light early warning system, aimed at alerting all healthcare providers (regardless of training) to vital sign abnormalities secondary to pre-eclampsia, maternal haemorrhage and sepsis. For pre-eclampsia, well-recognised thresholds for diagnosis have been selected for the thresholds triggering the lights (green = systolic BP < 140 mmHg and DBP < 90 mmHg, yellow = systolic BP 140–159 and/or diastolic BP

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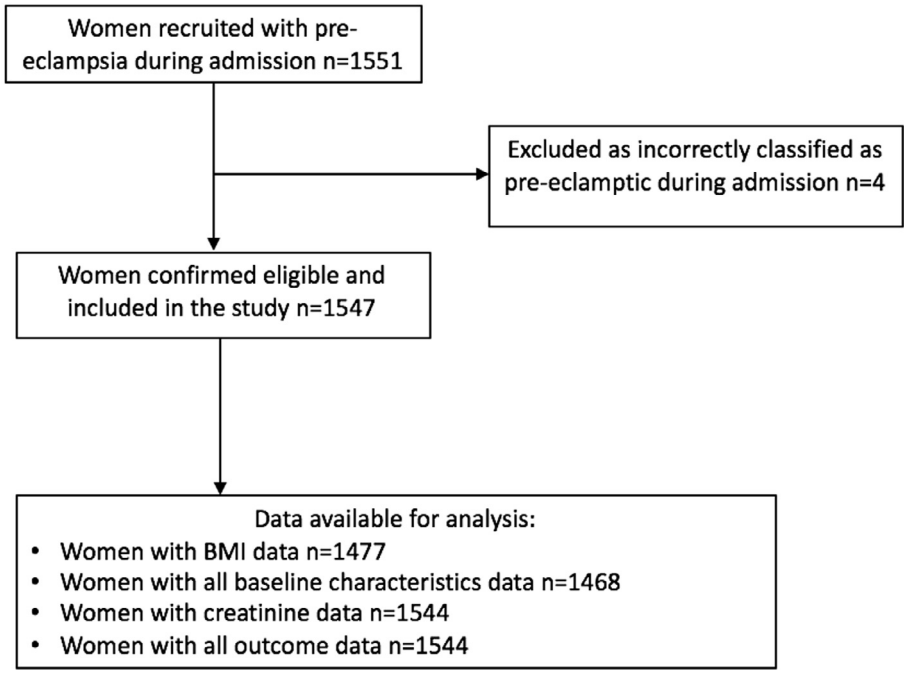

Fig. 1. Flow diagram of participants.

90–109 mmHg (but neither is above the upper threshold), red = systolic BP ≥160 mmHg and/or diastolic BP ≥ 110 mmHg) [9].

Although clinicians rely on these recommended BP thresholds to guide diagnosis and management of pre-eclampsia, the thresholds that indicate increased risk of complications of pre-eclampsia and (therefore dictate management) are based on expert opinion and limited data [9–14]. This study aimed to determine whether recommended BP thresholds (that trigger yellow and red lights in the CRADLE VSA) are associated with adverse outcomes in women with pre-eclampsia at facility-level in South Africa.

2. Methods

This prospective observational cohort study was undertaken between January 2015 and May 2016 at three state tertiary-level maternity units in South Africa (Groote Schuur, Tygerberg and Kimberley Hospitals). Women were eligible if they had a clinical diagnosis of pre-eclampsia during their admission. There were no exclusion criteria.

The study was approved by the Stellenbosch University Ethics Committee (N14/06068), University of Cape Town Ethics Committees (410/2014) and the University of the Free State Ethics Committee (230408-011). Local ethics committees at two of the three sites (Tygerberg Hospital and Kimberley Hospital) required individual informed written consent to be obtained before the woman was enrolled in the study (or waiver of consent was granted if the woman was unconscious). Institutional-level agreement for the study was given at the third site – Groote Schuur Hospital (i.e. individual-level consent was not required).

All BP devices in the three maternity units, except those within the anaesthetic and recovery areas, were replaced by the CRADLE Vital Signs Alert (VSA). Management protocols were unaltered.

BP on admission ('admission BP') and the highest BP during the course of the woman's hospital stay ('highest BP') were recorded for each woman. Pre-specified adverse clinical outcomes were recorded and included maternal outcomes (death, eclampsia, stroke, kidney injury), process measures (maternal use of magnesium sulfate, maternal Critical Care Unit (CCU) admission) and perinatal outcomes (extended perinatal death, delivery at < 34 weeks and < 37 weeks of gestation). Kidney injury was defined as highest creatinine during admission ≥90 μmol/L. Critical Care Unit admission was defined as admission to a critical care area providing at least additional monitoring and interventions [15]. Extended perinatal death included stillbirth, early neonatal and late neonatal death [16]. Data were extracted through patient notes reviewed by a local researcher and independently adjudicated. All women with pre-eclampsia were included but those with missing outcomes were excluded for that particular outcome analysis.

The primary analysis was the relationship between clinical outcomes to the BP thresholds that trigger the CRADLE VSA traffic light early warning system, using non-parametric trend testing [17], odds ratios (with 95% confidence intervals) and post-test probability (with 95% confidence intervals) for outcomes. Post-test probability (defined as the proportion of women triggering each traffic light who have the outcome) and odds ratios for yellow compared to green and red compared to yellow traffic lights were calculated. The post-test probability was reported rather than sensitivity, specificity, and positive and negative predictive values related to a single threshold (as recommended by Sackett et al.) [18] and 95% confidence intervals were included to allow for generalisation from the sample to the population with similar characteristics. The clinical outcomes associated with 'highest' SBP was assessed using Area Under the Receiver Operator Characteristic Curve (AUROC). Absolute differences in outcomes at increasing 'highest' SBP was illustrated using line graphs. Stepwise logistic regression analysis explored possible inflection points of 'admission' and 'highest' systolic and diastolic BP across the outcomes, including at the traffic light thresholds of SBP 140 mmHg, SBP 160 mmHg, DBP 90 mmHg and DBP 110 mmHg. For perinatal outcomes, an adjustment for clustering was made, using semi-robust standard errors, to allow for the inclusion of multi-fetal pregnancies.

A post-hoc power calculation for two principal outcomes (eclampsia and extended perinatal death) showed that the rate of eclampsia could be estimated to within 0.9% of the true value with 95% confidence and the rate of extended perinatal death could be estimated to within 1.3% of the true value with 95% confidence, based on incidence in previous literature [19]. Statistical analysis was performed in the statistical package Stata (version 11.2), College Station, TX. The study is reported in accordance with STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines.