Hypertension Research (2016) 39, 688–689

www.nature.com/hr

COMMENTARY

Maternal home blood pressure as a predictor of infant birth weight

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Hypertension Research (2016) **39,** 688–689; doi:10.1038/hr.2016.56; published online 19 May 2016

In this issue of the Journal, Iwama *et al.*[1] report the findings of a prospective study assessing the association between infant weight at birth and maternal blood pressure (BP), measured both in the clinic (CBP) and at home (HBP), between 10 and 20 weeks gestation in a large cohort of Japanese women. The authors found that increased diastolic and mean HBP values before 20 weeks gestation were related to a higher risk of lower infant birth weight than diastolic and mean CBP after adjusting for several confounders.

The clinical and prognostic value of BP measurements performed in different settings remains controversial.

Clinic BP measured by a physician in the office has long been considered the reference standard to quantify cardiovascular risk related to high BP and to select therapeutic strategies. A major limitation of CBP is the poor value of a single BP recording or a few BP recordings in predicting BP levels outside of the medical environment and in predicting subclinical cardiac and extra-cardiac damage and the risk of cardiovascular events. Two major factors have been proposed to explain the limited power of clinic BP in predicting cardiovascular outcomes: (1) poor reproducibility of CBP due to marked BP variability over time (that is, minute-to-minute, hour-to-hour, day-to-day and so on) and (2) alarm reactions elicited by the physician triggering transient BP increments in a significant fraction of subjects.[2]

Over the past 30 years, the increased availability of reliable automated and semi-automated devices has facilitated increased ambulatory BP monitoring and self BP measurements by patients at home or in work settings. The clinical and prognostic value of HBP measurement has been extensively evaluated. Numerous cross-sectional and longitudinal studies have reported that HBP, by providing BP recordings under relatively stable conditions in the absence of the so-called 'white coat effect', is superior to CBP in terms of reproducibility, correlation with organ damage and predictive value with respect to cardiovascular morbidity and mortality. The Pressioni Monitorate e Loro Associazioni (PAMELA) sample provided evidence that the risk of cardiovascular and all-cause death during a long follow-up period is more steeply related to ambulatory and HBP than to CBP.[3] Furthermore, HBP has been shown to be poorly influenced by the placebo effect and has been shown to improve patient compliance; finally, HBP allows the diagnosis of two conditions, masked hypertension and white coat hypertension, which would be undetectable by CBP measurement alone. Therefore, HBP is increasingly regarded as a useful complement to CBP in the clinical management of hypertensive subjects, including pregnant women, and as an important tool for clinical research.[4]

Pregnancy appears to be a cardiovascular 'stress test', and hypertension during pregnancy has been consistently linked to high perinatal morbidity and mortality. Comprehensive evaluations of BP status during pregnancy have relevant implications for public health.[5,6] Studies comparing clinic BP measurements with ambulatory BP monitoring have documented a high rate of false-negative (that is, masked hypertension) and false-positive (that is, white coat hypertension) diagnoses of hypertension in pregnant women. In particular, the prevalence of white coat hypertension, assessed by ambulatory BP monitoring or HBP compared with CBP, has been reported to be markedly high during pregnancy and to be associated with a favorable prognosis. In a study designed to assess the prevalence and prognosis of white coat hypertension detected by HBP monitoring telemetrically measured in pregnant women with recently discovered hypertension, the prevalence of this BP phenotype was 76%.[7] Notably, birth weight was higher in infants born to women with white coat hypertension than in their counterparts with sustained hypertension (3571 *vs.* 3045 g, $P<0.05$). In a prospective survey aiming to elucidate the association between clinic and ambulatory BP values and small-for-gestational-age (SGA) birth weight, Eguchi and coworkers enrolled 146 pregnant women undergoing routine medical visits for maternal check-up or suspected hypertension.[8] In multivariable logistic regression analyses adjusting for several confounders, such as age, body mass index, previous pregnancies, active smoking habits and BP lowering drugs, 24-h systolic BP was more closely associated with SGA birth weights (odds ratio (OR) for 10 mm Hg 1.74; 95% confidence interval (CI) 1.28–2.38; $P<0.001$) than CBP (OR 1.40; 95% CI 0.92–2.13; $P=0.11$). Similar results were observed when 24-h systolic BP was replaced with day-time systolic BP, night-time systolic BP and 24-h diastolic BP.

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Low birth weight has been documented to be associated with an increased risk of non-fatal and fatal cardiovascular events, as well as type 2 diabetes mellitus, in adult life. Intrauterine metabolic and physiologic alterations during fetal life have been hypothesized to result in an increased risk of later disease; alternatively, the so-called 'fetal insulin hypothesis' describes the role of genetic variants inherited by the fetus that may affect intrauterine growth and predispose offspring to cardiovascular and metabolic diseases in adult life. Increased BP levels have been hypothesized to impair the development of the placental villous tree and reduce placenta functional capacity, impairing fetal growth. In contrast, increased maternal BP levels have been hypothesized to be a consequence of reduced fetal growth and to have a compensatory role in the presence of inadequate placental perfusion.

Emerging evidence supports the view that low birth weight is related to the synergistic effects of several factors.[8] In a large population-based study of more than 14 000 Norwegian family units, Miklestad *et al.*[9] assessed the relationship between offspring birth weight for gestational age (GA) and cardiovascular risk factors in both parents. The authors found that offspring birth weight was inversely associated with paternal clinic BP, body mass index, waist circumference and abnormal glucose and lipid levels; for mothers, similar associations were observed for BP, whereas contrasting associations were found for glucose, lipids and body mass index. The paternal findings are in keeping with the hypothesis that genetic factors interplay with high maternal BP in determining SGA birth weight.

The report by Iwama *et al.*[1] provides a new piece of evidence regarding the association between maternal BP and infant birth weight in a selected group of 605 women with normal kidney function and no BP lowering medications (mean age 32 ± 5 years). The major findings of this study can be summarized as follows: (1) diastolic HBP was a better predictor of infant birth weight than diastolic CBP (a 1 s.d. increase in both parameters was associated with a 33 and 21% higher risk of birth weight reduction); (2) similar results were found for mean arterial pressure (30% higher risk for HBP and 16% for clinic BP); (3) no independent association was observed for systolic BP, measured either in clinic or at home, with infant birth weight. The predictive value of diastolic and mean BP remained significant after adjustment for several confounders known to influence birth weight, such as maternal age, pre-pregnancy body mass index, smoking status, gestational weight gain, family history of hypertension and infant sex.

These results in the pregnancy setting confirm and expand upon previous evidence regarding the greater value of HBP over clinic BP in predicting outcomes. The strengths and limitations of the present study deserve several comments, including the following: (I) the association of diastolic BP, but not systolic BP, with low birth weight and (II) the methods for home and clinic BP measurements.

First, the explanation provided by the authors that high diastolic BP, reflecting an abnormal increase in peripheral vascular resistance, may impair placental perfusion, resulting in low infant birth weight, has solid physiopathologic ground. As for the lack of an association between maternal systolic BP (clinic and home) and birth weight, this result should be taken with caution because BP was measured in a restricted gestational period (from 10 to 20 weeks). In the Avon Longitudinal Study of Parents and Children including 9697 women, a higher systolic, but not diastolic, clinic BP at baseline (8 weeks gestation) and greater increases in systolic and diastolic blood pressure between 18 and 36 weeks gestation were associated with lower offspring birth weight and SGA in adjusted models.[10] Second, an important criticism of the study by Iwama *et al.* is that clinic BP was measured only on two occasions in the majority of cases (12% of cases had a single BP measurement). Given the wide changes in BP that occur during a single visit and the decreases in office BP documented after repeated visits, reliable assessments of BP status should be based on several measurements. The number of measurements was much higher for home than for clinic BP (median 4 *vs.* 2 measurements) in the study; this difference may partly explain the superior performance of BP assessed at home compared with the clinic setting.

Despite these limitations, the study by Iwana *et al.* demonstrates the relevance of out-of-office BP in the risk assessment of adverse pregnancy outcomes, such as low infant birth weight. Future studies are needed to evaluate the accuracy of different methods of BP measurement (that is, clinic BP, HBP and ambulatory BP) in predicting pregnancy-related disorders.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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