

COMMENTARY

Is labor-onset hypertension a novel category among hypertensive disorders of pregnancy associated with adverse events in high-risk subjects? Lights and shadows

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Hypertensive disorders of pregnancy are a spectrum of diseases ranging from chronic and gestational hypertension to eclampsia. Hypertensive disorders are estimated to affect 6–8% of all pregnancies worldwide.^{1,2} Despite being the leading cause of maternal death and a major cause of maternal and perinatal morbidity, the mechanisms responsible for the pathogenesis of hypertensive disorders of pregnancy have not yet been thoroughly elucidated.

Pregnant women are a high-risk population for hypertensive disorders because, during pregnancy, several physiological changes can lead to increased stress on the cardiovascular system.³ Within the first trimester, the total intravascular volume increases, resulting in relative dilutional anemia. An increased intravascular volume associated with neurohormonal changes leads to vasodilation. At the same time, the maternal heart rate and, in turn, cardiac output increase.³ Overall, these hemodynamic changes improve placental perfusion, which works at low pressures and high fluxes to allow fetal growth (Figure 1). However, these adjustments to the pregnancy status can have significant consequences on the maternal blood pressure control. In this context, abnormal placentation is considered to be a key issue in the promotion of hypertensive disorders of pregnancy. In fact, aberrant

interaction between the fetus and mother and placental hypoperfusion trigger neurohormonal feedback that promotes hypertensive maternal responses aimed at preserving placental perfusion (Figure 1).³ Pre-gravid cardiovascular diseases, such as hypertension, obesity and diabetes, facilitate and/or exacerbate the development of these adverse events. Overall, these negative hemodynamic changes can prompt hypertensive disorders of pregnancy, such as gestational hypertension, preeclampsia, eclampsia and Hemolysis, Elevated Liver enzyme levels and Low Platelet count syndrome, as well as stroke and other cardiovascular diseases during pregnancy, delivery and the postpartum period (Figure 1).

The interesting study by Ohno *et al.*⁴ sought to clarify the perinatal outcomes and risk factors for hypertension that are first detected after the onset of labor. The study was conducted on a large population of Japanese parturient women not affected by gestational hypertensive disorders until childbirth. The authors found that nearly one-quarter of the study population developed hypertension during labor, and they identified age, body mass index, systolic blood pressure, proteinuria and severe edema as risk factors for severe/emergent labor-onset hypertension. The findings are interesting and quite innovative. Ohno *et al.* have first investigated, as the main outcome, the blood pressure changes during delivery. Moreover, the authors have suggested that labor-onset hypertension can be considered an independent category. In this context, there

are several classifications for hypertensive disorders during pregnancy. For instance, European guidelines identify four categories: pre-existing hypertension, gestational hypertension, pre-existing hypertension plus superimposed gestational hypertension with proteinuria, and antenatally unclassifiable hypertension (Figure 2).⁵ Despite some differences, none of the international guidelines have proposed labor-onset hypertension as an independent category. However, we believe that the intriguing hypothesis of Ohno *et al.* should be tested in larger, well designed studies. Furthermore, the biological mechanisms proving this suggestion should be investigated and elucidated.

Labor is a particular physiological situation involving major hemodynamic changes that can considerably affect blood pressure. To date, few studies have explored the pathways involved in blood pressure changes at delivery. In this context, Long *et al.*⁶ suggested that the activation of renin–angiotensin system at delivery is associated with higher blood pressure. At the same time, it is known that blood pressure rises as a result of the effect of uterine contractions, causing an increase in both stroke volume and heart rate.⁷ In addition, acute pain during labor may lead to a generalized increase in sympathetic nerve activity, which is responsible for a higher cardiac output and the elevation of blood pressure.⁸

Moreover, Ohno *et al.* have concluded that late-onset hypertension is a risk factor for emergent hypertension and is associated with

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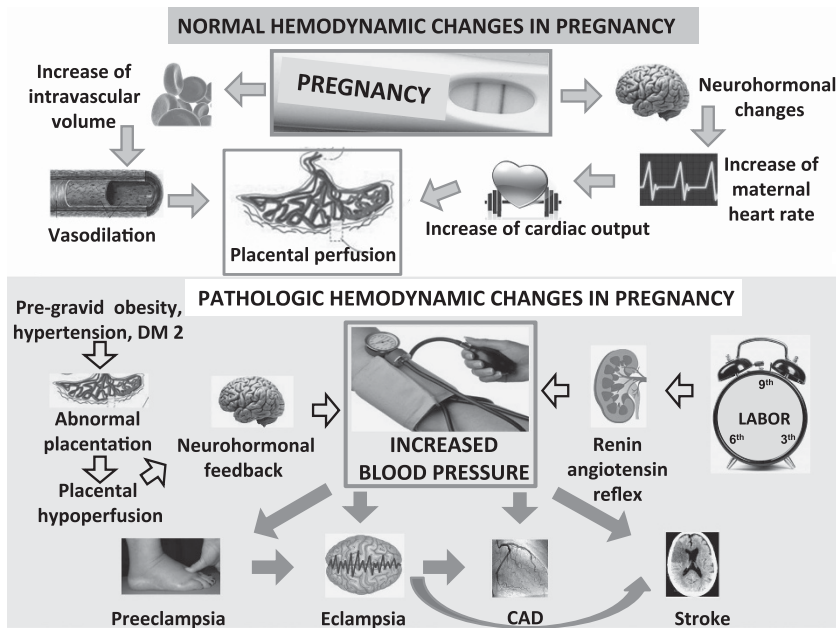


Figure 1 Physiological (above) and pathological (below) hemodynamic changes during pregnancy. CAD, coronary artery disease; DM 2, diabetes mellitus type 2.

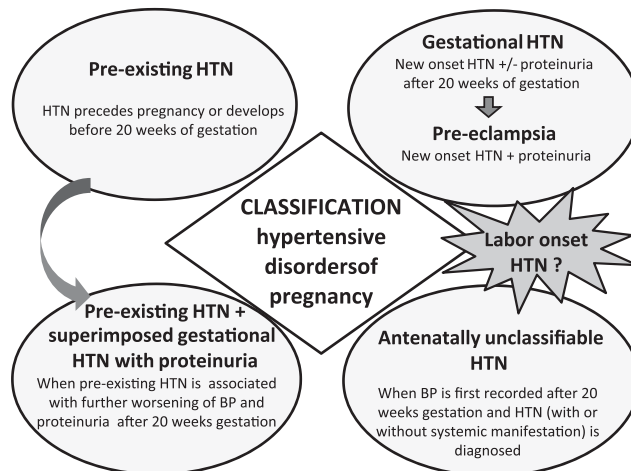


Figure 2 Classification of hypertensive disorders during pregnancy by the European Society of Cardiology. Is there a role for labor-onset hypertension? BP, blood pressure; HTN, hypertension (BP > 140/90); Proteinuria means ≥ 0.3 g per day in a 24-h urine collection or ≥ 30 mg mmol^{-1} urinary creatinine in a spot random urine sample.

eclampsia and stroke during the perinatal period. Similarly, high blood pressure levels have recently been associated with an increase in early postpartum preeclampsia. In a 6-month prospective observational study that included 1435 women, increased blood pressure values predicted the onset of early *de novo* postpartum preeclampsia in parturient women without any hypertensive disease during or before pregnancy.⁹ Recent studies have proposed anthropometric measurements (that is, body mass index and waist-to-hip ratio)¹⁰ and parameters of vascular function (central systolic pressure, augmentation index

and pulse wave velocity)^{11,12} as valid predictors of preeclampsia.

In the study by Ohno *et al.*,⁴ there are some limitations that merit mentioning. First, although it has been reported that eclampsia episodes and pregnancy-associated strokes often occur during labor and are associated with elevated blood pressure at delivery in the absence of any prior symptoms of hypertension or proteinuria,¹³ these associations are not sufficient to support that late-onset hypertension is a risk factor for eclampsia and stroke. Second, the size and homogeneity of the sample limit the generalizability of this

study. Finally, the study does not consider the administration of certain agents such as epidural analgesia and oxytocin, which may influence blood pressure during delivery. In particular, it has been reported that oxytocin moderately increases systolic blood pressure during labor.¹⁴ However, several studies have established that epidural block may cause a drop in the blood pressure values and may have a role in reducing the risk of late-onset hypertension.¹⁵ In keeping with these findings, it would be fascinating to explore the impact of these agents on blood pressure values and outcomes. In addition, on the basis of previous studies, the authors have suggested that the correct management of blood pressure during labor could reduce maternal deaths and strokes. Although few retrospective studies support this hypothesis, further investigations are required to identify the link between labor-onset hypertension and the risk of stroke to design an adequate treatment strategy.

In conclusion, although the clinical management of hypertension in pregnancy is well established,¹⁶ Ohno *et al.* have suggested a novel category of hypertension disorder, resulting in adverse pregnancy outcomes. As a result, their findings urge clinicians to promote the accurate measurement and prompt management of blood pressure during labor, especially in patients with risk factors for cardiovascular diseases, to reduce maternal and perinatal mortality and morbidity.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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