Editorial

Management of hypertension in pregnancy

Hypertensive disorders of pregnancy (HDP) constitute one of the leading causes of pregnancy related adverse outcomes worldwide (1). It has been estimated that HDP complicates up 5-10% of all pregnancies and this situation might worsen as a result of advanced age at first pregnancy and increased prevalence of obesity and other cardiometabolic risk factors among women of childbearing age (2, 3).

Affected women are also at increased risk for cardiovascular disease (CVD) later in life, independently of traditional cardiovascular disease risks (4).

In the primary healthcare setting prevention, timely diagnosis, and treatment of HDP are associated with reduced maternal, fetal and neonatal morbidity and mortality. Many international and national clinical practice guidelines and scientific statement have been published on this topic. The last one was Hypertension in Pregnancy: Diagnosis, Blood Pressure Goals, and Pharmacotherapy: A Scientific Statement from the American Heart association (AHA) in December 2021 (5).

Here we summarize the European Society of Cardiology (ESC) and the AHA scientific statement key diagnostic and treatment approaches to management HDP (Table 1).

ESC guideline for the management of cardiovascular diseases during pregnancy presents only a few focused recommendations in chapter Hypertensive disorders (7). The Scientific Statement from the American Heart Association is based on report of the American College of Obstetricians and Gynecologists task force on hypertension on pregnancy.

Analysis revealed consistency for the definitions of hypertension on pregnancy, chronic and gestational hypertension, and the preventive strategies of a low dose aspirin for women at increased risk of preeclampsia, antihypertensive treatment of hypertension, delivery for women with preeclampsia.

Significant variations include: different aspirin doses for prophylaxis of eclampsia, definitions of preeclampsia that reflect evolving of the multisystem nature of the disease, different antihypertensive treatment thresholds and targets among women with non-severe HDP, and postpartum monitoring for maternal safety and improvement of long-term cardiovascular health.

These variations arise from limited evidence to drive clinical practice and reflect the reality that many aspects of the guidelines emanate from expert opinion rather than high quality evidence. These are areas requiring further research and consensus-building for optimizing management of a high-risk group of women.

Since the main differences are related to the target blood pressure (BP) level, here the arguments for tight and less tight BP control in pregnancy from the AHA scientific statement.

Arguments in favor of a tight BP control in pregnancy

First, there are no measurable immediate or long-term health benefits of stricter BP treatment for the relatively short duration of pregnancy (4–9 months, depending on type of HDP) in young women without other CVD risks.

Second, there are concerns that lowering maternal BP may compromise utero-placental circulation and negatively affect fetal well-being and growth.

Third, therapeutic options are limited because of concerns about potential adverse fetal effects, particularly malformations from intrauterine exposure to antihypertensive medications.

Arguments for considering tight BP control

First, more aggressive treatment of hypertension in pregnancy prevents the development of severe hypertension, as demonstrated by both a systematic review of randomized trials (8) and Control of Hypertension in Pregnancy Study (CHIPS) (9).

Second, there is evidence that the women with preeclampsia may be more susceptible to severe neurological outcomes such as intracerebral hemorrhage at lower systolic BP (e.g, 150–170 mmHg) compared with nonpregnant subjects.

Third, treatment of nonsevere hypertension in pregnancy (e.g, BPs 140–155/90–109 mmHg) may permit prolongation of pregnancy in women without other severe features of preeclampsia who would require delivery.

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Table 1. Hypertension in Pregnancy: Summary of the ESC guideline and a Scientific Statement from the AHA		
Parameter	**ESC, 2018**	**AHA, 2021**
Threshold for the diagnosis	Office (or in-hospital) SBP ≥140 mmHg and/or DBP ≥ 90 mmHg	BP ≥140/90 mmHg; 2 elevated BP measurements 4 hours apart.
Severe hypertension	≥160/110mmHg	≥160/110mmHg
Blood pressure measurement	Mercury sphygmomanometers; Oscillometric automatic devices validated in pregnant women; Ambulatory BP monitoring is superior to routine BP measurement for the prediction of pregnancy outcome.	Mercury sphygmomanometers; Oscillometric automated devices validated in pregnant women; Self-monitoring may be equivalent to standard clinic thresholds.
Classification	-Pre-existing hypertension; -Gestational hypertension; -Pre-eclampsia; -Preexisting hypertension plus superimposed gestational hypertension with proteinuria; -Antenatally unclassifiable hypertension	-Preeclampsia/eclampsia; -Chronic hypertension (of any cause); -Chronic hypertension with superimposed preeclampsia; -Gestational hypertension
Treatment threshold	≥150/95 mmHg; >140/90 mmHg in women with: - gestational hypertension (with or without proteinuria); - pre-existing hypertension with the superimposition of gestational hypertension; - with subclinical organ damage or symptoms	≥160/110 mm Hg if acute/chronic hypertension Consider lower treatment threshold if co morbidities or renal failure is present and to consult with other subspecialties about BP targets.
Treatment target	<140/90 mm Hg, but noting the optimal BP target in pregnancy is unknown	120-159/80-105 mm Hg
Proteinuria	Dipstick reading of ≥1+, should prompt further investigations: random urine albumin/creatinine ratio ≥30mg/mmol	≥300 mg in a 24-hour urine collection or protein/creatinine ratio ≥0.3 mg/dL or Dipstick reading of 2+ (used only if other quantitative methods not available)(6)
Preeclampsia diagnosis	-Gestational hypertension with significant proteinuria; -Hypertension is accompanied by headache, visual disturbances, abdominal pain, or abnormal laboratory tests, specifically low platelets and/or abnormal liver function.	Does not require proteinuria, based on maternal end-organ involved: thrombocytopenia (<100000x10^9/L), elevated blood concentrations of liver enzymes (to twice the upper limit normal concentration), progressive renal insufficiency (creatinine >1.1 mg/dL or doubling in the absence of other renal disease), pulmonary edema, or new-onset cerebral or visual disturbances. Fetal manifestation are not specified
Superimposed pre-eclampsia on chronic hypertension	Hypertension <20 week of gestation+ superimposed gestational hypertension+proteinuria	Chronic hypertension + new proteinuria after 20 weeks; sudden substantial and sustained increase in proteinuria; sudden increase in BP or need to increase antihypertensive dose; sudden signs and symptoms maternal end-organ involved (see above)
Treatment threshold	≥140/90 mmHg	≥160/110 mmHg

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Parameter	**ESC, 2018**	**AHA, 2021**
Treatment target	<140/90 mm Hg, but noting the optimal BP target in pregnancy is unknown	Non severe preeclampsia <160/110 mm Hg Chronic hypertension 120-159/80-104 mmHg
Urgent treatment of severe hypertension	-Intravenous labetalol (C), oral methyldopa (B) or nifedipine (C); -Intravenous hydralazine; -Intravenous Uradipil; -Nitroglycerin when preeclampsia is associated with pulmonary edema (C).	-Intravenous labetalol (C); -Intravenous hydralazine; - nifedipine, immediate release(C);
Antihypertensive treatment	methyldopa (B), labetalol (C), and calcium antagonists (C)	labetalol (C), methyldopa (B), nifedipine (C);
Prediction and prevention of preeclampsia	Screening by high and moderate clinical risk markers; Low dose aspirin (100-150 mg daily) is recommended in women at high or moderate risk of pre-eclampsia from week 12 to weeks 36–37; Calcium supplementation (1,5–2 g/day) in women with low dietary intake of calcium (<600mg/day)	Screening by clinical assessment (high, moderate); Low-dose aspirin (81 mg/day) prophylaxis is recommended in women at high risk of preeclampsia and should be initiated between 12 weeks and 28 weeks of gestation (optimally before 16 weeks) and continued daily until delivery.
Delivery	-Gestational hypertension or mild pre-eclampsia, delivery is recommended at 37 weeks; -Preeclampsia with adverse conditions is recommended to expedite delivery	-37 weeks gestation for women with gestational hypertension and preeclampsia without severe features; -Women with severe features preeclampsia should be delivered at 34 week; -Indication for earlier delivery (prior to fetal viability) if maternal end-organ involved (6)
Postpartum hypertension	-	Hypertension (usually mild) that develops 2weeks to 6 months postpartum, usually normalizing by the end of the first year
Postpartum CVD risk management	Annual visits to a primary care physician to check BP and metabolic factors are recommended	Postpartum follow-up visit with either the primary care professional or cardiologist is recommended within 7-10 days of delivery
BP – blood pressure, CVD – cardiovascular disease, DBP – diastolic blood pressure, SBP – systolic blood pressure		

Fourth, ACOG guidelines recommend withholding antihypertensive therapy for patients with preeclampsia unless BP approaches 160/110 mmHg. They also recommend urgent delivery for women with severe features of preeclampsia, which include uncontrollable hypertension with BP ≥160/110 mmHg, even for pregnancies <34 gestational weeks, unless high-level care is available in facilities with adequate maternal and neonatal intensive care resources (10). Lowering thresholds for treatment may allow timely BP control and avoidance of rushed deliveries that commonly lead to prematurity and related complications.

Fifth, there are current epidemiological and demographic trends toward advanced age at first pregnancy and higher CVD risk (subclinical or diagnosed). This could also be relevant among women with multiple pregnancies, who may spend several years of their lives either pregnant or breastfeeding with uncontrolled hypertension. In addition, modern fertility techniques facilitate pregnancy in women with preexisting conditions associated with elevated CVD risk (diabetes, chronic kidney disease, and polycystic ovary syndrome). Preexisting chronic kidney disease and heart disease are present in 3% and 1% to 4% of pregnancies in high-income countries, respectively (11).

Finally, there is abundant evidence that HDP are associated with increased risk of both immediate and postpartum complications and future maternal vascular disease. Whether better management of BP during pregnancy will lead to lower rates of morbidity related to hypertension in the immediate postpartum period is not known. It is estimated that approximately two-thirds of HDP-associated CVD risk is mediated by established risk factors, and the remainder is likely explained by an HDP specific pathogenesis (12).

Given the current situation, AHA endorses informed decision-making in partnership with the patient as to whether to treat nonsevere hypertension during pregnancy to targets similar to those recommended in nonpregnant individuals. Personalization of therapy, by giving special attention to other risk factors related to hypertension-related adverse outcomes (such as preexisting heart or kidney disease, obesity, and Black race), is a rational approach.

Management of hypertension in pregnancy requires multidisciplinary collaborations among obstetricians, maternal fetal medicine specialists, neonatologists, nephrologists and hypertension specialists, cardiologists, anesthesiologists, pharmacists, nurses, and midwives, all of whom contribute to providing cohesive and safe preconception, antepartum, peripartum, and postpartum care.

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