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PREECLAMPSIA (VD GAROVIC, SECTION EDITOR)

Prevention, Diagnosis, and Management of Hypertensive Disorders of Pregnancy: a Comparison of International Guidelines

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Abstract

Purpose of Review Hypertensive disorders of pregnancy (HDP)—gestational hypertension, preeclampsia, and eclampsia—are a leading cause of adverse maternal and perinatal outcomes internationally. Prevention, timely diagnosis, and prompt management can reduce associated morbidity. The purpose of this review is to compare international guidelines pertaining to HDP.

Recent Findings Fourteen HDP guidelines were compared relative to guidelines for the United States (US) where the authors practice. Aspirin is universally recommended for high-risk women to reduce preeclampsia risk. Recommended dose and gestational age at initiation vary. Diagnoses of chronic hypertension, gestational hypertension, and preeclampsia in pregnant women are similar, although blood pressure (BP) thresholds for antihypertensive medication initiation and treatment targets vary due to the limitations in high-quality evidence.

Summary There are differences among international HDP guidelines related to dose and timing of aspirin initiation, thresholds for antihypertensive medication initiation, and BP targets. However, all guidelines acknowledge the significant morbidity associated with HDP and advocate for timely diagnosis and management to reduce associated morbidity and mortality. More research is needed to understand optimal BP thresholds at which to initiate antihypertensive medication regimens and BP targets in pregnancy.

Keywords Chronic hypertension · Eclampsia · Gestational hypertension · Guidelines · Hypertensive disorders of pregnancy · Preeclampsia

Introduction

Globally, hypertensive disorders of pregnancy (HDP) are a leading cause of morbidity, mortality, hospitalization, and resource utilization for both mothers and their neonates [1–5]. In developed countries, HDP are often diagnosed at routine prenatal care visits, as many women are asymptomatic at the time of diagnosis. Prenatal care affords the opportunity of prevention, early diagnosis, management and treatment of HDP. Conversely, women without prenatal care may present with more advanced disease, such as eclampsia, the most severe form of preeclampsia characterized by generalized tonic-clonic seizures and associated with even higher morbidity and mortality [6, 7]. Adherence to a HDP protocol is associated with reduced maternal morbidity and mortality [8–10]. Therefore, in this review we compare international guidelines for the prevention, diagnosis, and management of HDP through the clinical lens of practice in the United States (US) where the authors practice (Fig. 1).

This article is part of the Topical Collection on *Preeclampsia*

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Fig. 1 Current hypertension guidelines

American College of Obstetricians and Gynecologists

In 2019, the American College of Obstetricians and Gynecologists (ACOG) published updated guidelines on the diagnosis and management of chronic hypertension, gestational hypertension and preeclampsia [11••, 12••]. Prevention of preeclampsia is the first goal, and ACOG outlined recommendations for the use of low-dose aspirin for preeclampsia prophylaxis in a separate committee opinion published in 2018 [13]. Aspirin 81 mg is recommended for high-risk women (among other groups) between 12 and 28 weeks gestation (Table 1).

ACOG defines chronic hypertension as hypertension diagnosed before pregnancy or before 20 weeks gestation with blood pressure (BP) ≥ 140/90 mmHg on at least 2 occasions 4 or more hours apart. They cite new diagnostic criteria for stage 1 hypertension–systolic blood pressure (SBP) 130–139 mmHg or diastolic blood pressure (DBP) 80–89 mmHg–from the 2017 American College of Cardiology/American Heart Association guideline [14•], but they state that the significance of these parameters in pregnancy is not certain. ACOG recommends maintaining BP < 160/110 mmHg with labetalol and nifedipine, the two first-line oral agents for long-term control (Table 2).

ACOG distinguishes gestational hypertension from preeclampsia. Gestational hypertension is defined as new onset hypertension with BP ≥ 140/90 on 2 occasions at least 4 h apart after 20 weeks gestation. Preeclampsia is defined as hypertension with proteinuria or other end-organ effects, including thrombocytopenia < 100×10^9/L, renal insufficiency with serum Cr > 1.1 mg/dL or doubling from baseline, impaired liver function with transaminases greater than twice normal, pulmonary edema, and new onset headache unresponsive to medications or visual symptoms. In both chronic hypertension and gestational hypertension, ACOG recommends antihypertensive medications when BP ≥ 160/110 mmHg with goal BP below this threshold. Intravenous hydralazine and labetalol and oral nifedipine are recommended for acute hypertensive urgency, and oral labetalol and calcium channel blockers are recommended for long-term control.

ACOG specifies that outpatient management is an option for women diagnosed with gestational hypertension or preeclampsia without severe features dependent on adherence to frequent outpatient visits. Hospitalization is recommended until delivery for those with severe disease (end-organ damage or severe hypertension) and for those who cannot undergo close outpatient monitoring. ACOG recommends fetal growth ultrasound measurements every 3–4 weeks, measurement of amniotic fluid at least weekly and antenatal testing once or twice weekly. Delivery is recommended at 37 weeks gestation for women with gestational hypertension and preeclampsia without severe features and at 34 weeks for women with preeclampsia with severe features. Indications for earlier delivery include uncontrolled severe-range BP, refractory headaches or upper abdominal pain, visual disturbances, stroke, myocardial infarction, hemolysis elevated liver enzyme low platelet

Table 1 Aspirin: preeclampsia risk-reducing recommendations by hypertension guideline

Guideline	Year	Daily dose	GA (weeks)		Who qualifies
			Begin	End	
ACOG	2019	81 mg	12–28	Delivery	≥ 1 high risk factor (1), or > 1 moderate risk factor (2)
USPSTF	2017	81 mg	12		≥ 1 high risk factor (1)
WHO	2011	75 mg	< 20		≥ 1 high risk factor (1, 3)
NICE	2019	75–150 mg	12	Delivery	≥ 1 high risk factor (4), or > 1 moderate risk factor (5)
ESC/ESH	2018	100–150 mg	12	36	High (4) or moderate (5) risk
Ireland	2019	75–100 mg	12–16	Delivery	≥ 1 high risk factor (4), or > 1 moderate risk factor (5)
FIGO	2019	150 mg	11–14	36, or delivery, or preeclampsia	High risk (locally defined), or Risk ≥ 1 in 100
Queensland	2016	100 mg	< 16	37, or delivery	Moderate to high risk (6)
SOMANZ	2014	Low dose		37	Moderate to high risk (7)
ISSHP	2018	75–162 mg	16–20		Strong risk factors (8)
Brazil	2016	75–150 mg	12		Intermediate or increased risk (9)
DGGG	2015	100 mg		Up to 34	
ACC/AHA	2017	No specific recommendation, refer to ACOG recommendations			
Canada	2018	No recommendations			

(1) High risk factors (per ACOG, USPSTF, WHO): history of preeclampsia, multi-fetal gestation, chronic hypertension, type 1 or 2 diabetes, renal disease, autoimmune disease

(2) Moderate risk factors (per ACOG): nulliparity, obesity (BMI > 30), preeclampsia in the patient's mother or sister, African American race, low socioeconomic status, age > 35 years, history of a small for gestational age neonate, previous adverse pregnancy outcome, or > 10 year pregnancy interval

(3) USPSTF notes these risk factors are not exhaustive but do not specify further. They also note aspirin may be beneficial as early as 12 weeks gestation)

(4) High risk factors (per NICE, ESC/ESH, Royal College of Physicians of Ireland): hypertensive disease during previous pregnancy, chronic kidney disease, autoimmune disease, type 1 or 2 diabetes, chronic hypertension

(5) Moderate risk factors (per NICE, ESC/ESH, Royal College of Physicians of Ireland): first pregnancy, age ≥ 40, pregnancy interval > 10 years, BMI ≥ 35 at first visit, family history of preeclampsia, multi-fetal pregnancy

(6) Queensland risk factors (not differentiated between moderate and high risk): antiphospholipid antibodies, previous history of preeclampsia, pre-existing diabetes, twin pregnancy (increased risk with multiples), nulliparity, family history of preeclampsia, BMI > 35 before pregnancy or at initial visit, age > 40, SBP >130 and DBP >80 at initial visit, inter-pregnancy interval > 10 years, renal disease, chronic autoimmune disease, chronic hypertension

(8) ISSHP strong risk factors: prior preeclampsia, chronic hypertension, pre-gestational diabetes, renal disease, maternal BMI > 30, multiple pregnancy, antiphospholipid syndrome, assisted reproduction pregnancy. ASA used to prevent preterm but not term preeclampsia

(7) SOMANZ risk factors (not differentiated between moderate and high risk): nulliparity, multiple pregnancy, previous history of preeclampsia, family history of preeclampsia, BMI ≥ 25, age ≥ 40, SBP >130 or DBP > 80 before 20 weeks, antiphospholipid syndrome, pre-existing diabetes, renal disease, chronic autoimmune disease, inter-pregnancy interval > 10 years

(9) Not specified

For blank cells, no specific recommendation is provided by the respective guideline

(HELLP) syndrome, worsening renal dysfunction, pulmonary edema, eclampsia or fetal distress (such as abnormal fetal testing or reversed end-diastolic flow in the umbilical artery), among others. Magnesium sulfate is recommended for women with preeclampsia with severe features for eclampsia prophylaxis during labor and delivery and continued until 24 h postpartum.

American College of Cardiology/American Heart Association

The 2017 American College of Cardiology/American Heart Association (ACC/AHA) guideline [14•] states that "It is beyond the scope of the present guideline to address the management of hypertension during pregnancy in detail" and

Table 2 Antepartum antihypertensive medication initiation and blood pressure goals by hypertensive disorder of pregnancy guideline and/or country

Guideline and/or country	Recommended medication initiation (mmHg)	Target BP (mmHg)
ACOG [11••, 12••]	≥ 160	< 160
	≥ 110	< 110
ISSHP [15]	≥ 140	110–140
	≥ 90	85
Queensland [16]	≥ 140	< 140
	≥ 90	< 90
Canada [17]	≥ 140	NR
	≥ 90	85
SOMANZ [18]	≥ 160	< 160
	≥ 110	< 110
Brazil [19]	> 150	130–150
	> 100	80–100
Germany [20]	≥ 150	< 150
Ireland [16, 19]	≥ 100	80–100
NICE [21]	≥ 140	135
	≥ 90	85
ESC/ESH [22]	≥ 150	< 140
	≥ 95	< 90

Top number in each cell = systolic BP, bottom number = diastolic BP. *BP* blood pressure, *NR* no recommendation

refers readers to the 2013 ACOG [23] and 2011 European Society of Cardiology (ESC) Cardiovascular Diseases during Pregnancy [24] guidelines. The 2017 ACC/AHA Guideline makes two specific recommendations for the treatment of hypertension in pregnancy:

1. "Women with hypertension who become pregnant, or are planning to become pregnant, should be transitioned to methyldopa, nifedipine, and/or labetalol during pregnancy."
2. "Women with hypertension who become pregnant should not be treated with ACE inhibitors, ARBs, or direct renin inhibitors."

The guideline states that the reasons for antihypertensive treatment during pregnancy are twofold: first, to prevent severe hypertension; second, to potentially prolong pregnancy for fetal benefit. The guideline cites the United States Preventive Services Task Force (USPSTF) recommendation for universal BP measurement of every pregnant woman at every prenatal visit [25]. It recommends that in women with hypertensive crises, for example severe preeclampsia or eclampsia, SBP should be reduced to < 140 mmHg during the first hour of treatment. This may differ from usual clinical practice, as an abrupt reduction of mean arterial pressure may lead to a reduction in fetal perfusion and an abnormal fetal heart rate tracing, leading to urgent fetal delivery.

US Preventive Services Task Force

The United States Preventive Task Force (USPSTF) made two major recommendations pertaining to preeclampsia. In 2014, they endorsed low-dose aspirin 81 mg for preeclampsia prevention in high-risk women (Table 1) [26], reversing their 1996 statement that there was "insufficient [evidence] to assess the balance of benefits and harms of aspirin use to prevent preeclampsia in pregnant women at increased risk for preeclampsia." [27] They stated that there are minimal harms of low-dose aspirin in pregnancy, and that "there is a substantial net benefit of daily low-dose aspirin to reduce the risk for preeclampsia, preterm birth, and fetal growth restriction in women at high risk for preeclampsia."

In 2017, the USPSTF recommended screening for preeclampsia with BP measurements in all pregnant women since knowledge of elevated BP can allow for timely diagnosis and treatment, including close maternal and fetal surveillance, antihypertensive medications and magnesium sulfate for eclampsia prophylaxis [28].

World Health Organization

The World Health Organization (WHO) published the Prevention and Treatment of Pre-eclampsia and Eclampsia guideline in 2011 [29]. Although the guideline references chronic hypertension, gestational hypertension, preeclampsia, and eclampsia, there was no specific mention of diagnostic criteria for these conditions. The document contains 23 recommendations designated as "recommended" or "not recommended." The 2 recommendations with both a high quality of evidence and a strong strength of recommendation are (1) magnesium sulfate is the drug of choice for eclampsia prophylaxis, and (2) vitamin C and E should not be used for preeclampsia prevention. Both of these recommendations are based on robust clinical trial evidence. The WHO meticulously detailed the trials supporting these and other recommendations in a separate document with 59 tables summarizing the evidence [30]. The other 21 recommendations are broadly grouped into preeclampsia prevention, management of HDP and hemolysis elevated liver enzymes low platelet (HELLP)

syndrome and timing of delivery. For preeclampsia prevention, they advise calcium supplementation during pregnancy in areas with low dietary calcium intake and low-dose aspirin 75 mg daily initiated prior to 20 weeks gestation for high-risk women. They advise against several interventions that have not been shown to reduce the risk of preeclampsia, including resting at home or strict bedrest, restriction of salt intake or supplementation of vitamin D. They advise pharmacologic treatment of severe hypertension during pregnancy and postpartum and state that the choice of medication should be based on the physician's experience with the specific medication, medication cost and local availability. They specifically advise against diuretics for the prevention of preeclampsia and do not recommend corticosteroids for treating HELLP syndrome.

WHO recommends delivery for women with severe preeclampsia when the fetus is not viable or unlikely to be viable in another 1–2 weeks. Expectant management (delaying delivery until maternal and/or fetal decline or a pre-specified gestational age) is recommended in patients with severe preeclampsia before 34 weeks of gestation (without other indication for delivery), and expectant management of severe preeclampsia may be offered up to 36 weeks 6 days in the absence of uncontrolled hypertension, end-organ damage, or fetal distress. This recommendation was reaffirmed in 2018, albeit as a "conditional recommendation" with "very low certainty evidence." [31] Importantly, this differs significantly from the ACOG recommendation of delivery at 34 weeks gestation in women with severe preeclampsia. Other than this difference, the WHO recommendations generally align with US practice. WHO recommends delivery at term in gestational hypertension, mild preeclampsia, and severe preeclampsia. No recommendations are made on outpatient versus inpatient management or on fetal surveillance.

International Federation of Gynecology and Obstetrics

The International Federation of Gynecology and Obstetrics (FIGO) defers to the International Society for the Study of Hypertension in Pregnancy (ISSHP) for specific recommendations related to the diagnosis and treatment of HDP, but they do present a separate guideline for first-trimester screening for prevention of preeclampsia [32]. This guideline is largely based on the body of work published by Nicolaides and colleagues [33]. The global panel of authors outline the evidence advocating for screening for and prevention of preterm preeclampsia, defined as preeclampsia with delivery < 34 weeks gestation. They advocate for universal preeclampsia screening, stating that the best combined test includes "maternal risk factors, mean arterial pressure, placental growth factor and uterine artery pulsatility index" as a one-step procedure. For high-risk women, defined as risk of developing preeclampsia ≥ 1 in 100, they recommend aspirin 150 mg nightly. This recommendation is in contrast to that of ACOG [11••], which cites a low positive predictive value as the primary reason that tests such as placental growth factor and uterine artery Doppler measurements should remain investigational [11••]. Differences in these guidelines appear to stem from varying opinions on acceptable sensitivity/specificity levels of screening tests, costs associated with screening, and limited interventions for high-risk women beyond routinely prescribed low-dose aspirin. Implementing an additional sonogram in a US cohort of 4 million annual births [34] would increase healthcare expenditures by millions of dollars; the exact return on investment should be examined with a cost-effectiveness analysis.

International Society for the Study of Hypertension in Pregnancy

In 2018, the International Society for the Study of Hypertension in Pregnancy (ISSHP) issued a statement on classification, diagnosis, and management recommendations for international practice, endorsed by the International Society for Obstetric Medicine and the Study of Hypertension in Pregnancy [15]. The panel of authors includes members from Australia, the UK, Ireland, US, Japan, South Africa, and Nigeria. Overall, the recommendations for management mirror those of ACOG with minor variations. The one significant difference centers on BP thresholds for antihypertensive medication initiation and BP treatment goals. The ISSHP recommends that BP ≥ 140/90 mmHg (or ≥ 135/85 mmHg at home) should be treated with a goal BP 110–140/85 mmHg (Table 2). The rationale provided is to reduce the risk of "severe hypertension and other complications such as low platelets and elevated liver enzymes with symptoms." The ISSHP acknowledges the lack of high-quality randomized controlled trials (RCTs) and that this recommendation stems from a single trial that compared tight to less-tight control in women with HDP [35]. In this trial, the incidence of severe hypertension was higher in women randomized to less-tight control (aOR 1.80 (95% CI 1.34–2.38)), but there was no difference in the composite adverse perinatal outcome (aOR 1.02 (95% CI 0.77–1.35)) or in serious maternal complications (aOR 1.74 (95% CI 0.79–3.84)). Given the critical need for high-quality evidence, the senior authors of the current review article (AT and SO) are actively enrolling women in the Chronic Hypertension and Pregnancy (CHAP) Project, a large, multicenter RCT to assess benefits and harms of treatment of mild hypertension in pregnancy (NCT02299414). Study results are expected in 2022. Current differences between guidelines for blood pressure thresholds and management may originate from varying opinions over what level of evidence is necessary to inform practice.

Hypertension Canada

Hypertension Canada's 2018 Guidelines for the Management of Hypertension in Pregnancy, developed in conjunction with the Society of Obstetricians and Gynaecologists, are the inaugural guideline for the management of hypertension in pregnancy in Canada [17]. They present 7 recommendations for the management of hypertension in pregnancy. The definitions of various forms of HDP align with those used in the US. The main difference relates to the management of non-severe hypertension, which aligns with ISSHP guidelines. Hypertension Canada's Pregnancy Guidelines recommend antihypertensive therapy for non-severe hypertension (SBP ≥ 140 mmHg or DBP ≥ 90 mmHg) with a goal DBP of 85 mmHg (Table 2) for women on antihypertensives and women with preeclampsia, but acknowledge that the limited data supporting this recommendation are limited.

Society of Obstetric Medicine of Australia and New Zealand

The Society of Obstetric Medicine of Australia and New Zealand (SOMANZ) Guideline for the Management of Hypertensive Disorders of Pregnancy was published in 2014 [18]. Diagnostic criteria are similar to those used in the US. While they do not endorse the "30-15 rule," a principle prompting preeclampsia evaluation in women not meeting traditional diagnostic thresholds but with SBP ≥ 30 mmHg or DBP ≥ 15 mmHg above patient's baseline BPs, they state that a "30-15" BP rise combined with elevated uric acid, proteinuria, or fetal growth restriction may warrant monitoring. An additional difference lies in treatment of severe hypertension, defined as BP ≥ 160/110. SOMANZ recommends treating severe hypertension but states that BPs ≥ 170/110 mmHg require urgent treatment. This differs only slightly from the ACOG "Committee Opinion on Emergent Therapy for Acute-Onset, Severe Hypertension During Pregnancy and Postpartum" that advises an aggressive treatment approach at a threshold of ≥ 160/110 mmHg [36].

In contrast to previously mentioned guidelines, SOMANZ pays specific attention to the psychosocial impact of preeclampsia on the patient and her family. The guideline states that "the woman and her family are often overwhelmed and distressed from their experience and appropriate management postpartum should include psychological and family support." SOMANZ highlights engaged patient advocacy organizations such as the Australian Action on Preeclampsia (AAPEC) and New Zealand Action on Preeclampsia (NZ APEC) groups. In the US, ACOG has a history of collaboration with the Preeclampsia Foundation (https://www.preeclampsia.org/), a leading voice of advocacy for women with preeclampsia, but does not officially address the psychosocial impact of preeclampsia or formally endorse any support organizations in its guidelines [11••].

Queensland Maternity and Neonatal Clinical Guideline

The Queensland Maternity and Neonatal Clinical Guideline was published in 2016. [16] Diagnostic criteria for chronic hypertension and gestational hypertension generally mirror those of ACOG. The preeclampsia prophylaxis recommendations differ from ACOG by advising aspirin 100 mg daily. They succinctly define preeclampsia as a "multi-system disorder characterized by hypertension and involvement of one or more other organ systems and / or the fetus." Similar to SOMANZ, they address the "30-15" rule in noting that, while not diagnostic, a patient with a "30-15" elevation in BP should undergo prompt clinical and laboratory assessment for preeclampsia.

Similar to ISSHP, they recommend considering antihypertensive medication for SBP ≥ 140–160 mmHg or DBP ≥ 90–100 mmHg (Table 2). Postpartum, they recommend treating to achieve target BPs < 140/90. They state that provider familiarity and experience should guide choice of antihypertensive medication. Inpatient management is recommended for BPs > 140/90 mmHg, presence of signs and symptoms of preeclampsia or concern for fetal well-being. Interestingly, they describe a management category entitled "Day stay," allowing for heightened outpatient surveillance in eligible patients. A "day stay" involves "frequent maternal and fetal surveillance … with daily review by an obstetrician" as compared with 24-h in-hospital observation.

Brazilian Guideline of Arterial Hypertension

In 2016, the 7th Brazilian Guideline of Arterial Hypertension was published, including a chapter specifically discussing the management of hypertension in pregnancy. [19] HDP definitions are similar to those in the US. The guideline recommends low-dose aspirin 75–150 mg for preeclampsia prevention in women at intermediate or high risk (Table 1). They recommend treatment with antihypertensive medications for BP > 150/100 mmHg in chronic hypertension, gestational hypertension and preeclampsia (Table 2). Intravenous hydralazine is the preferred agent for urgent pharmacologic treatment, whereas oral agents for long-term control include methyldopa, B-blockers (except atenolol), hydralazine, and calcium channel blockers (nifedipine, amlodipine, and verapamil). They target a goal BP of 130–150/80–100 mmHg and recommend that women with gestational hypertension and non-severe preeclampsia may be managed by "day-hospital with monitoring," while women with severe hypertension should

be managed in the hospital with relative rest. The guideline acknowledges a lack of evidence to support a specific inpatient approach but recommends periodic BP assessment, daily weight and diuresis assessment, maternal laboratory evaluation 1–2 times per week and fetal surveillance. The guideline recommends expectant management until 36 weeks for women with gestational hypertension and without clinical worsening or severe hypertension. No specific recommendations for delivery in women with severe preeclampsia are provided. They highlight the dilemma surrounding the ideal delivery time in severe preeclampsia before 32–34 weeks and the high neonatal survival rates after 34 weeks gestation. For women with severe preeclampsia, magnesium sulfate is recommended for eclampsia prevention during labor and for approximately 24 h postpartum. An "attack" dose of 4-6 g intravenously followed by 1–3 g/h maintenance is recommended.

German Society of Gynecology and Obstetrics

In 2015, the German Society of Gynecology and Obstetrics (DGGG) published guidelines for the diagnosis and treatment of hypertensive disorders in pregnancy [20]. HDP definitions mirror those published by ACOG. One notable difference lies in the DGGG recommendation of a target BP of < 150/80–100 mmHg with alpha-methyldopa as the first-line antihypertensive agent (Table 2). Other medications considered partially suitable include nifedipine and selective β1 receptor blockers, with metoprolol preferred in this class. The guideline suggests consideration of dose reduction or discontinuation of antihypertensive medications depending on physiologic changes in BP in the first half of pregnancy, given the potential fetal harm with overtreatment.

The DGGG guidelines recommend referral to the hospital for BP ≥ 150/100 mmHg or signs and symptoms suggestive of preeclampsia. They recommend that medications only be initiated in the hospital and only when BP ≥ 150/100 mmHg, but state that treatment can be withheld as long as BP is < 160/110 mmHg. For treatment of acute severe hypertension, nifedipine, and urapidil are preferred first-line treatment. The DGGG guideline outlines recommendations for inpatient fetal surveillance with cardiotocography 1–3 times per day and fetometry every 10–14 days with measurement of amniotic fluid. They do not provide recommendations for outpatient management. Women with severe preeclampsia are recommended to deliver after 34 weeks. Women with mild preeclampsia are recommended to deliver at 37 weeks provided there are no signs or symptoms of end-organ dysfunction. DGGG recommends magnesium sulfate to prevent eclamptic seizures in women with severe preeclampsia, noting that its utility among women with preeclampsia without severe features is under discussion. Typically, a loading dose of 4–6 g is administered over 15–20 min, followed by a maintenance dose of 1 g/h, continued for up to 48 h postpartum.

Institute of Obstetricians and Gynaecologists, Royal College of Physicians of Ireland

The Institute of Obstetricians and Gynaecologists, Royal College of Physicians of Ireland provides two technical bulletins on HDP: "The Management of Hypertension in Pregnancy" published in 2016 and revised in 2019, [16] and "The Diagnosis and Management of Severe Preeclampsia and Eclampsia" published in 2011 and revised in 2016 [19]. The guidelines are derived from a systematic review of the literature from 2000 to 2015. For preeclampsia prevention, they recommend low-dose aspirin (75 mg) for prophylaxis and calcium supplementation for women with poor dietary calcium intake (Table 1). They note that preeclampsia rarely presents before 20 weeks and highlight the importance of measuring BP with a cuff validated in pregnancy, as discussed in a recent systematic review [37]. They discuss preconception counseling in women with chronic hypertension and emphasize the importance of optimizing modifiable risk factors prior to pregnancy. They specify that women with a history of hypertension > 4 years duration should undergo maternal echocardiogram to assess left ventricular function.

A key addition to the diagnostic criteria that differs from other guidelines is the inclusion of a "moderate" hypertension classification (in addition to mild and severe), defined as SBP 150–159 mmHg or DBP 100–109 mmHg. They recommend pharmacologic treatment for moderate hypertension with target SBP < 150 mmHg and DBP 80–99 mmHg for women without medical comorbidities (Table 2). For women with underlying comorbidities, such as diabetes or renal disease, they recommend tighter control with goal SBP < 140 and DBP 80–99 mmHg. They recommend postpartum target BP < 150/80–99 mmHg for women without significant comorbidities and BP < 140/80–90 mmHg for women with comorbidities.

National Institute for Health and Care Excellence

The National Institute for Health and Care Excellence (NICE) Hypertension in Pregnancy: Diagnosis and Management guideline was published in 2019 in the UK [21]. Overall, the NICE guideline is similar to ACOG. Differences include antihypertensive therapy for women with chronic hypertension with BPs persistently ≥ 140/90 (Table 2). Women with gestational hypertension and preeclampsia not already treated should be offered medication following birth if BP ≥ 150/110. Target BP is 135/85 in all HDP patients. NICE advocates

for placental growth-factor (PlGF)–based testing to help rule out preeclampsia, while ACOG does not. Since 79% of screen positive PIGF patients do not develop HDP, ACOG cites a low positive predictive value (21.2%) as rationale for not incorporating PIGF into clinical practice [11••].

European Society of Cardiology/European Society of Hypertension

The 2018 European Society of Cardiology/European Society of Hypertension Guidelines were published in the UK in 2018 as a collaboration of experts across Europe. They make specific recommendations for HDP similar to ACOG [22]. Variations include recommending a higher dose of aspirin of 100–150 mg for preeclampsia prevention (Table 1) and initiation of antihypertensives for BPs persistently ≥ 150/95 (Table 2). Following initiation of treatment, they suggest a target BP of < 140/90, noting that the optimal BP target in pregnancy is unknown. They recommend that Doppler ultrasound of the uterine arteries can be utilized after 20 weeks gestation to detect higher risk of intrauterine growth retardation. This practice is not endorsed by ACOG given the absence of effective interventions [11••].

Conclusion

International guidelines on the prevention, diagnosis, and management of HDP are remarkably similar. They acknowledge the significant complications of unrecognized and untreated HDP and the opportunity to improve outcomes through a combination of prevention, timely diagnosis, prompt treatment, and delivery when indicated. Significant variations in guidelines include different prophylaxis recommendations, such as aspirin dose, timing of initiation, and candidacy (Table 1) and different antihypertensive treatment thresholds and targets (Table 2). These discrepancies stem from limitations in high-quality evidence supporting any particular approach, varying opinions of acceptable sensitivity/specificity thresholds for screening tests, cost implications, and limited availability of effective interventions. Additional international inconsistencies include antihypertensive medication recommendations, use of sonography for surveillance, recommended treatment, and gestational age at delivery for women with preeclampsia and preeclampsia with severe features. 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.

Ongoing and future research will continue to inform development of new HDP guidelines. Areas with limited information and, thus, lack of clear guidance include racial differences in antihypertensive response in pregnancy, interventions to reduce racial disparities in HDP-related maternal mortality [38], timely management of severe hypertension in women with difficult intravenous access and optimal psychosocial support for families of women with a preeclampsia diagnosis. Meanwhile, adherence to universal BP screening at prenatal and postpartum visits and to a protocol that promotes early diagnosis and treatment are the gold standards to reduce the morbidity and mortality of HDP [39, 40].

Compliance with Ethical Standards

Conflict of Interest The authors declare no conflicts of interest relevant to this manuscript.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
- •• Of major importance

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