Brief Review

Hypertensive Disorders of Pregnancy

ISSHP Classification, Diagnosis, and Management Recommendations for International Practice

Mark A. Brown, Laura A. Magee, Louise C. Kenny, S. Ananth Karumanchi, Fergus P. McCarthy, Shigeru Saito, David R. Hall, Charlotte E. Warren, Gloria Adoyi, Salisu Ishaku; on behalf of the International Society for the Study of Hypertension in Pregnancy (ISSHP)

These recommendations from the International Society for the Study of Hypertension in Pregnancy (ISSHP) are based on available literature and expert opinion. It is intended that this be a living document, to be updated when needed as more research becomes available to influence good clinical practice. Unfortunately, there is a relative lack of high-quality randomized trials in the field of hypertension in pregnancy compared with studies in essential hypertension outside of pregnancy, and ISSHP encourages greater funding and uptake of collaborative research in this field. Accordingly, the quality of evidence for the recommendations in this document has not been graded although relevant references and explanations are provided for each recommendation. The document will be a living guideline, and we hope to be able to grade recommendations in the future.

Guidelines and recommendations for management of hypertension in pregnancy are typically written for implementation in an ideal setting. It is acknowledged that in many parts of the world, it will not be possible to adopt all of these recommendations; for this reason, options for management in less-resourced settings are discussed separately in relation to diagnosis, evaluation, and treatment.

This document has been endorsed by the International Society of Obstetric Medicine and the Japanese Society for the Study of Hypertension in Pregnancy.

Key Points

All units managing hypertensive pregnant women should maintain and review uniform departmental management protocols and conduct regular audits of maternal and fetal outcomes.

The cause(s) of preeclampsia and the optimal clinical management of the hypertensive disorders of pregnancy remain uncertain; therefore, we recommend that every hypertensive pregnant woman be offered an opportunity to participate in research, clinical trials, and follow-up studies.

Classification

1. Hypertension in pregnancy may be chronic (predating pregnancy or diagnosed before 20 weeks of pregnancy) or de novo (either preeclampsia or gestational hypertension).
2. Chronic hypertension is associated with adverse maternal and fetal outcomes and is best managed by tightly controlling maternal blood pressure (BP, 110–140/85 mmHg), monitoring fetal growth, and repeatedly assessing for the development of preeclampsia and maternal complications. This can be done in an outpatient setting.
3. White-coat hypertension refers to elevated office/clinic (≥140/90 mmHg) BP, but normal BP measured at home or work (<135/85 mmHg); it is not an entirely benign condition and conveys an increased risk for preeclampsia.
4. Masked hypertension is another form of hypertension, more difficult to diagnose, characterized by BP that is normal at a clinic or office visit but elevated at other times, most typically diagnosed by 24-hour ambulatory BP monitoring (ABPM) or automated home BP monitoring.
5. Gestational hypertension is hypertension arising de novo after 20 weeks’ gestation in the absence of proteinuria and without biochemical or hematological abnormalities. It is usually not accompanied by fetal growth restriction. Outcomes in pregnancies complicated by gestational hypertension are normally good, but about a quarter of women with gestational hypertension (particularly those who present at <34 weeks) will progress to preeclampsia and have poorer outcomes.
6. Preeclampsia is a complex medical disorder; worldwide, each year, it is responsible for >500,000 fetal and neonatal deaths and >70,000 maternal deaths. Preeclampsia can deteriorate rapidly and without warning; we do not recommend classifying it as mild or severe.
7. Proteinuria is not mandatory for a diagnosis of preeclampsia. Rather, this is diagnosed by the presence of de novo hypertension after 20 weeks’ gestation accompanied by proteinuria and/or evidence of maternal acute kidney injury (AKI), liver dysfunction, neurological features, hemolysis or thrombocytopenia, or fetal growth restriction. Preeclampsia may develop or be recognized for the first time intrapartum or early postpartum in some cases.

8. The hemolysis, elevated liver enzymes, low platelets syndrome is a (serious) manifestation of preeclampsia and not a separate disorder.

**Diagnosis of Hypertension and Proteinuria**

1. Home BP monitoring is a useful adjunct in the management of chronic hypertension and is mandatory in the management of white-coat hypertension.

2. Proteinuria is optimally assessed by screening with automated dipstick urinalysis and then if positive quantifying with a urine protein/creatinine ratio. A ratio ≥30 mg/mmol (0.3 mg/mg) is abnormal.

**Prediction and Prevention of Preeclampsia and Associated Complications**

1. No first or second trimester test or set of tests can reliably predict the development of all cases of preeclampsia; however, a combination of maternal risk factors, BP, placental growth factor (PIGF), and uterine artery Doppler can select women who may benefit from 150 mg/d of aspirin to prevent preterm (before 37 weeks gestation) but not term preeclampsia. ISSHP supports first trimester screening for risk of preeclampsia when this can be integrated into the local health system although the cost effectiveness of this approach remains to be established.

2. ISSHP recommends that women with established strong clinical risk factors for preeclampsia (ie, prior preeclampsia, chronic hypertension, pregestational diabetes mellitus, maternal body mass index >30 kg/m², antiphospholipid syndrome, and receipt of assisted reproduction) be treated, ideally before 16 weeks but definitely before 20 weeks, with low-dose aspirin (defined as 75–162 mg/d, as studied in randomized controlled trials).

3. We recommend at this stage against the routine clinical use of rule-in or rule-out tests (specifically PIGF or sFlt-1 [soluble fms-like tyrosine kinase-1/PIGF ratio]) for preeclampsia, which should continue to be evaluated within the context of clinical trials.

4. Women considered at increased risk for preeclampsia as above should receive supplemental calcium (1.2–2.5 g/d) if their intake is likely to be low (<600 mg/d), in addition to aspirin. When intake cannot be assessed or predicted, it is reasonable to give calcium.

5. Low molecular weight heparin is not indicated to prevent preeclampsia, even with a history of prior early onset preeclampsia.

6. Women should exercise during pregnancy to maintain health, appropriate body weight, and reduce the likelihood of hypertension.

**Management**

1. Regardless of the hypertensive disorder of pregnancy, BP requires urgent treatment in a monitored setting when severe (>160/110 mmHg); acceptable agents for this include oral nifedipine or intravenous labetalol or hydralazine. Oral labetalol may be used if these treatments are unavailable.

2. Regardless of the hypertensive disorder of pregnancy, BPs consistently at or >140/90 mmHg in clinic or office (or ≥135/85 mmHg at home) should be treated, aiming for a target diastolic BP of 85 mmHg in the office (and systolic BP of 110–140 mmHg) to reduce the likelihood of developing severe maternal hypertension and other complications, such as low platelets and elevated liver enzymes with symptoms. Antihypertensive drugs should be reduced or ceased if diastolic BP falls <80 mmHg. Acceptable agents include oral methyl dopa, labetalol, oxprenolol, and nifedipine, and second or third line agents include hydralazine and prazosin.

3. Women with preeclampsia should be assessed in hospital when first diagnosed; thereafter, some may be managed as outpatients once it is established that their condition is stable and they can be relied on to report problems and monitor their BP.

4. Women with preeclampsia who have proteinuria and severe hypertension, or hypertension with neurological signs or symptoms, should receive magnesium sulfate (MgSO₄) for convulsion prophylaxis.

5. Fetal monitoring in preeclampsia should include an initial assessment to confirm fetal well-being. In the presence of fetal growth restriction, a recommended schedule for serial fetal surveillance with ultrasound is detailed within these recommendations.

6. Maternal monitoring in preeclampsia should include BP monitoring, repeated assessments for proteinuria if BPs consistently at or >140/90 mmHg in clinic or office (or ≥135/85 mmHg at home) or intravenous labetalol or oral nifedipine, and if severe hypertension develops, oral or parenteral magnesium sulfate is recommended. Women with preeclampsia should be assessed in hospital when first diagnosed; thereafter, some may be managed as outpatients once it is established that their condition is stable and they can be relied on to report problems and monitor their BP.

7. Women with preeclampsia should be delivered if they have reached 37 weeks’ (and zero days) gestation or if they develop any of the following:

   - Repeated episodes of severe hypertension despite maintenance treatment with 3 classes of antihypertensive agents;
   - Progressive thrombocytopenia;
   - Progressively abnormal renal or liver enzyme tests;
   - Pulmonary edema;
   - Abnormal neurological features, such as severe intractable headache, repeated visual scotomata, or convulsions;
   - Nonreassuring fetal status.

**Postpartum Care**

1. In the early postpartum period, women with preeclampsia should be considered at high risk for preeclamptic complications for at least 3 days and should have their BP and clinical condition monitored at least every 4 hours while awake. Antihypertensives administered antenatally should be continued, and consideration should...
be given to treating any hypertension before day 6 postpartum with antihypertensive therapy. Therefore, antihypertensive therapy may be withdrawn slowly over days but not ceased abruptly. It is important to note that eclamptic seizures may develop for the first time in the early postpartum period.

2. Nonsteroidal anti-inflammatory drugs (NSAIDs) for postpartum analgesia should be avoided in women with preeclampsia unless other analgesics are not working; this is especially important if they have known renal disease, or preeclampsia is associated with placental abruption, AKI, or other known risk factors for AKI (eg, sepsis, postpartum hemorrhage).

3. All women should be reviewed at 3 months postpartum to ensure that BP, urinalysis, and any laboratory abnormalities have normalized. If proteinuria or hypertension persists, then appropriate referral for further investigations should be initiated.

4. There are significant long-term cardiovascular risks for women with chronic hypertension and those who have had gestational hypertension or preeclampsia. One initial recommendation may be to aim to achieve prepregnancy weight by 12 months and to limit interpregnancy weight gain through healthy lifestyle.

5. Annual medical review is advised life-long, and all such women should adopt a healthy lifestyle that includes exercise, eating well, and aiming for ideal body weight.

### Introduction

Worldwide there is disagreement about many aspects of the classification, diagnosis, and management of the hypertensive disorders of pregnancy. This lack of consensus hampers our ability to study not only the immediate rates of adverse maternal and fetal outcomes for the various hypertensive disorders in pregnancy, particularly preeclampsia, but also the long-term health outcomes of women and babies who survive this condition. It also impacts on research into the pathophysiology of this condition and has almost certainly delayed the development of effective screening tests and treatments, leading to poorer pregnancy outcomes.

One scholarly review of available guidelines has shown broad agreement in the following areas:

1. Definitions of preeclampsia, proteinuria, chronic hypertension, and gestational hypertension;
2. Prevention of preeclampsia with low-dose aspirin and supplemental calcium (if low calcium intake);
3. Treatment of severe hypertension;
4. Use of MgSO4 for eclampsia and severe preeclampsia;
5. Use of antenatal corticosteroids to enhance fetal lung maturity at <34 weeks’ gestation if delivery is likely within the next 7 days;
6. Delivery for preeclampsia at term; and
7. Oxytocin in the third stage of labor.

However, in this analysis, there was little or no agreement on

1. The definition of preeclampsia;
2. Target BP when hypertension is not severe;
3. Timing of delivery for women with chronic hypertension, gestational hypertension, or preterm preeclampsia;
4. Use of MgSO4 for preeclampsia that is not severe; and
5. Postpartum maternal monitoring.

After the 2016 World Congress of the ISSHP, it was agreed that a single up-to-date guideline should be available that reflects current evidence, and both the collective expertise of the ISSHP membership and the leadership role that ISSHP would like to take in improving hypertension-related outcomes in pregnancy. After the Congress, ISSHP charged a small group of clinician researchers to update the last statements from ISSHP 2013 and 2014.2,3

This set of recommendations provides practical advice on classification, diagnostic criteria, and management for all clinicians, everywhere, who are involved in the management of women with hypertension in pregnancy.

### Section 1. Classification of the Hypertensive Disorders of Pregnancy

The recommended classification for hypertensive disorders of pregnancy is as follows:

| Hypertension known before pregnancy or present in the first 20 weeks |
|--------------------------|------------------|
| Chronic hypertension     |
| Essential                |
| Secondary                |
| White-coat hypertension  |
| Masked hypertension      |
| Hypertension arising de novo at or after 20 weeks |
| Transient gestational hypertension |
| Gestational hypertension |
| Preeclampsia* de novo or superimposed on chronic hypertension |

*The term severe preeclampsia should not be used in clinical practice.

### Notes

1. Preeclampsia, transient gestational hypertension, and gestational hypertension are characterized by the new onset of hypertension (BP ≥140 mm Hg systolic or ≥90 mm Hg diastolic) at or after 20 weeks’ gestation; as such, it is important to have normal BP documented either prepregnancy or in early pregnancy before there has been much pregnancy-related decrease in BP. Otherwise, a BP first measured after 12 weeks’ gestation that is normal may reflect the usual fall in BP from baseline that occurs by the end of the first trimester; in which case, there may still be underlying chronic hypertension that has been masked by this first trimester BP fall.

2. Transient gestational hypertension is hypertension that arises in the second or third trimester. The hypertension is usually detected in the clinic but then settles with repeated BP readings, such as those taken during the course of several hours in a day assessment unit. This differs from white-coat hypertension that, by definition, must be present from early pregnancy. Transient gestational hypertension is associated with a 40% risk of developing true gestational hypertension or preeclampsia in the remainder of the pregnancy, a fact that highlights the importance of carefully following-up such women.

3. When a woman presents with hypertension in pregnancy at or after 20 weeks’ gestation and the earlier BP is
unknown, she should be managed in pregnancy as if she has gestational hypertension or preeclampsia. Appropriate investigations should be done after pregnancy to determine whether she has underlying chronic hypertension. This will generally be apparent because the BP will not have normalized within 3 months postpartum.

4. Masked hypertension is another form of hypertension, characterized by BP that is normal at a clinic or office visit but elevated at other times, most typically diagnosed by 24-hour ABPM or automated home BP monitoring. Such a diagnosis is generally sought when a patient has unexplained abnormalities consistent with target organ damage from hypertension but no apparent hypertension. Although this is a form of chronic hypertension, the prevalence of masked hypertension and its significance in pregnancy are less well studied; for now, we do not recommend seeking this diagnosis in the absence of the above features (ie, unexplained chronic kidney disease [CKD], left ventricular hypertrophy, or retinopathy recognized early in pregnancy).

5. Although ISSHP has formerly published a statement documenting severe preeclampsia, we agree with the position of American College of Obstetricians and Gynecologists (ACOG) and others that preeclampsia may become a major threat to mother and baby at any stage, and classification into mild or severe disease can be erroneous or misleading to less experienced clinicians. ACOG has eliminated the diagnosis of severe hypertension1 and classification into mild or severe disease can now, we do not recommend seeking this diagnosis in the absence of the above features.

### Section 2. Diagnosis of the Hypertensive Disorders of Pregnancy

#### What Constitutes Hypertension in Pregnancy?

<table>
<thead>
<tr>
<th>Hypertension</th>
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<tbody>
<tr>
<td>Defined as systolic BP ≥140 and/or diastolic BP ≥90 mmHg.</td>
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<tr>
<td>BP should be repeated to confirm true hypertension.</td>
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<td>If BP is severe (systolic BP ≥160 and/or diastolic BP ≥110 mmHg), then the BP should be confirmed within 15 minutes;</td>
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<tr>
<td>For less severe BP, repeated readings should be taken for a few hours.</td>
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<tr>
<td>Use a liquid crystal sphygmomanometer.</td>
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<td>If this is unavailable, use a validated and appropriately calibrated automated device.</td>
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### Notes

1. Mercury sphygmomanometry is no longer available. The alternative may be a liquid crystal sphygmomanometer,4 but these are not yet widely available. Correct cuff size is important, using a large cuff if the mid upper arm circumference is >33 cm.

2. Aneroid devices are used commonly for BP measurement, but they may be inaccurate and need to be regularly calibrated. One smaller study found that 50% of aneroid devices had at least 1 BP reading >10 mm Hg out compared with the same error in only 10% of mercury devices.5

3. Use of an automated device is preferable to use of an aneroid device if the automated device has been shown to be reliable in both pregnancy and preeclampsia specifically6,7; some devices may be accurate for women with chronic or gestational hypertension in pregnancy but not for women with preeclampsia.8 A list of generally validated home BP monitors, not specific for pregnancy, is available at http://bbsoc.org/bp-monitors/bp-monitors/.

#### What Constitutes Abnormal Proteinuria in Pregnancy?

- Proteinuria should be assessed initially by automated dipstick urinalysis when possible; if not available, careful visual dipstick urinalysis will suffice.
- If positive (≥1+, 30 mg/dL), then spot urine protein/creatinine (PCr) ratio should be performed.
- A PCr ratio ≥30 mg/mmol (0.3 mg/mg) is abnormal.
- A negative dipstick test can usually be accepted, and further PCr testing is not required at that time.
- Proteinuria is not required for a diagnosis of preeclampsia.
- Massive proteinuria (>5 g/24 h) is associated with more severe neonatal outcomes.

### Notes

1. The gold standard for diagnosing abnormal proteinuria in pregnancy is a 24-hour urinary protein ≥300 mg per day although this is more a time-honored value than one with high scientific proof;11 ideally, 24-hour creatinine excretion will also be used to assess adequacy of collection as without this, the estimated daily urine protein excretion is often incorrect.12

2. In practice, the 24-hour urine protein measurement will mostly be replaced with a spot urine protein/creatinine ratio, a value ≥30 mg per mmol (≥0.26 mg/mg, usually rounded to 0.3 mg/mg) representing significant proteinuria13–15; this eliminates the inherent difficulties in undertaking 24-hour urine collections and speeds up the process of decision making.

3. Twenty-four–hour urine collection for proteinuria is still indicated to confirm nephrotic syndrome which has implications for thromboprophylaxis.

4. Dipstick testing is not perfect, and a small number of proteinuric cases may be missed by a negative dipstick test; a urine PCr <30 mg/mmol also occasionally gives a false-negative result for abnormal 24-hour proteinuria, but in such cases, the total protein excretion is usually <400 mg/d.14

5. At present, there is insufficient data to recommend using urinary albumin/creatinine ratio, but this may change when more research becomes available13,16 such as the results of Diagnostic Accuracy in Preeclampsia using Proteinuria Assessment (RCTN82607486).

6. When neither 24 hour nor PCr measures of proteinuria are available, dipstick testing provides reasonable assessment of true proteinuria, particularly when values are >1 g per liter, that is, 2+.15,17

7. There is ongoing debate on the importance of the absolute quantification of proteinuria. Some think that the degree of proteinuria provides little additional risk stratification (except in nephrotic syndrome), and it should not be included in considerations of the severity of preeclampsia.15,18–20 Others have shown that massive proteinuria (>5 g/24 h) is associated with more severe
neonatal outcomes and earlier delivery, and a spot PCr >900 mg/mmol (or >500 mg/mmol if age >35 years) is associated with worse maternal outcomes.²¹,²² For this reason, some units may choose to continue measuring proteinuria although it is not recommended that a decision to deliver is based on the degree of proteinuria.

8. If proteinuria is diagnosed but subsequent dipstick tests become negative, then further quantification tests are appropriate to see whether or not true proteinuria persists.

9. In recent years, gestational proteinuria has been recognized as a real entity. It is unclear exactly how many pregnancies are affected by this condition, defined as the new onset of proteinuria in pregnancy without other obvious features of preeclampsia or primary renal disease. Women with gestational proteinuria have blood levels of placental growth factor that are intermediate between those of normal pregnancies and preeclampsia, prompting consideration that these women have an early form of preeclampsia.²³ The recommended approach to management of these women is to consider 3 possible outcomes.

- No features of preeclampsia develop throughout pregnancy and proteinuria disappears postpartum;

- Proteinuria turns out to be the first feature of preeclampsia, which is defined when the BP subsequently rises or other features of preeclampsia develop;

- The proteinuria persists postpartum and ultimately signifies a primary renal disease that has coincidentally developed in the pregnancy, an unusual event.

It is, therefore, recommended to monitor these women more frequently than usual for the remainder of their pregnancy, as well as to assess proteinuria at 3 months postpartum.

Notes

1. Many women will not have had their BPs measured within months before becoming pregnant. In practice therefore, we rely mostly on the first trimester BP to define normal or high BP.

2. Up to 1 in 4 patients with elevated clinic or office BP have white coat hypertension. This diagnosis can be avoided in large part by having clinic or office BP recorded by a nurse, rather than a doctor, preferably using repeated BP readings.²⁴ We recommend that all women have either home BP monitoring monitoring or 24-hour ABPM before a diagnosis of true essential hypertension is accepted.

3. Normal values for 24-hour ABPM in pregnancy have been determined;²⁵ before 22 weeks, BP values should be below: 24-hour average 126/76 mmHg; awake average BP 132/79 mmHg; sleep average BP 114/66 mmHg. These values are slightly lower than those used as thresholds for diagnosing hypertension in nonpregnant women.

4. Most automated home BP devices are accurate in pregnancy, but ≥25% differ from standard sphygmomanometry devices;²⁶ therefore, all women should have their home BP device checked (against a calibrated sphygmomanometer or automated device validated for use in pregnancy and preeclampsia) before using that device. In the absence of severe hypertension (>160/110 mmHg), we suggest relying on average BP over several days rather than acting on single readings for women monitoring home BP values.

5. Most cases of chronic hypertension are because of essential hypertension, usually accompanied by a family history of hypertension and often by overweight or obesity.

6. Secondary causes of hypertension are less common; in the age group of women who conceive, the cause is usually an underlying primary renal parenchymal disorder (such as reflux nephropathy or glomerulonephritis) and less commonly, fibromuscular hyperplasia of the renal arteries or primary hyperaldosteronism. ISSHP does not recommend routine testing for any secondary cause of hypertension in the absence of clinical clues to these conditions.

ISSHP recommends that all women with chronic hypertension in pregnancy have the following tests performed at first diagnosis. This will provide a baseline reference should suspicion arise later in pregnancy of superimposed preeclampsia (which will complicate up to 25% of these pregnancies).

1. A full blood count (hemoglobin and platelet count).

2. Liver enzymes (aspartate aminotransferase, alanine aminotransferase, and lactate dehydrogenase) and functions tests (international normalized ratio, serum bilirubin, and serum albumin).

3. Serum creatinine, electrolytes, and uric acid (Serum uric acid is not a diagnostic criterion for preeclampsia, but elevated gestation-corrected uric acid serum levels are associated with worse maternal and fetal outcomes and should prompt a detailed assessment of fetal growth, even in women with gestational hypertension. However, uric acid should not be used to determine the timing of delivery.).

4. Urinalysis and microscopy, as well as PCr or albumin: creatinine ratio.

- Renal ultrasound if serum creatinine or any of the urine testing are abnormal.

Notes

1. Transient gestational hypertension is not a benign disorder; it is associated with ≥20% chance of developing...
preeclampsia and a further 20% chance of developing gestational hypertension. Therefore, such women should receive extra monitoring throughout their pregnancy, ideally including home BP measurements.

<table>
<thead>
<tr>
<th>Gestational Hypertension (Gestational Hypertension)</th>
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<tr>
<td>Gestational hypertension is persistent de novo hypertension that develops at or after 20 weeks’ gestation in the absence of features of preeclampsia.</td>
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**Notes**

1. Gestational hypertension is not a uniformly benign condition. The risk of complications is dependent on the gestational age at which it develops. Gestational hypertension is important for 2 reasons:
   - Preeclampsia may develop in 25% of such women, and this rate being higher the earlier the presentation; to date, no tests have reliably predicted which women with gestational hypertension will later develop preeclampsia.
   - Gestational hypertension, like preeclampsia, is also associated with cardiovascular disease in the long term.

<table>
<thead>
<tr>
<th>Preeclampsia</th>
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<tr>
<td>Preeclampsia is gestational hypertension accompanied by ≥1 of the following new-onset conditions at or after 20 weeks’ gestation:</td>
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<tr>
<td>Proteinuria</td>
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<td>Other maternal organ dysfunction, including:</td>
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<tr>
<td>AKI (creatinine ≥90umol/L; 1 mg/dl)</td>
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<tr>
<td>Liver involvement (elevated transaminases, eg, alanine aminotransferase or aspartate aminotransferase &gt;40 IU/L) with or without right upper quadrant or epigastric abdominal pain</td>
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<td>Neurological complications (examples include eclampsia, altered mental status, blindness, stroke, clonus, severe headaches, and persistent visual scotomata)</td>
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<tr>
<td>Hematological complications (thrombocytopenia–platelet count &lt;150 000/μL, disseminated intravascular coagulation, hemolysis)</td>
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<tr>
<td>Uteroplacental dysfunction (such as fetal growth restriction, abnormal umbilical artery [UA] Doppler wave form analysis, or stillbirth)</td>
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</table>

**Notes**

1. Hyper-reflexia occurs in many women with preeclampsia and resolves postpartum. However, it is a nonspecific finding that is often present in otherwise well young women and is highly subject to observer interpretation. Therefore, ISSHP no longer recommends including this in the diagnostic criteria.

2. Headaches in pregnancy are multifactorial. However, in the presence of hypertension, a new headache should be considered to be part of preeclampsia until proved otherwise; this is a safe clinical approach.

3. Proteinuria is not required for a diagnosis of preeclampsia but is present in ≥75% of cases.

4. When resources are available, all asymptomatic women with de novo hypertension and no dipstick proteinuria should have the following laboratory investigations performed to evaluate maternal organ dysfunction. Without these, it will be impossible to exclude preeclampsia. In some countries, this approach will necessitate referral of patients (of whom some will not have preeclampsia) from smaller units where same-day laboratory facilities are not available. Local decision-making strategies will be necessary in these areas.

   - Hemoglobin, platelet count (and if decreased, tests of coagulation)
   - Serum creatinine
   - Liver enzymes
   - Serum uric acid

   Hemolysis, elevated liver enzymes, low platelets: The combination of all or some of hemolysis, elevated liver enzymes and thrombocytopenia is often referred to as the HELLP syndrome. For clinicians familiar with the management of preeclampsia, this constellation of abnormalities signifies a more serious part of the spectrum of this disorder. However, it is still considered part of preeclampsia and not a separate disorder. ISSHP endorses this approach to reduce confusion among those less familiar with the multisystem complications that might occur in preeclampsia. In other words, women with features of HELLP syndrome should be considered to have preeclampsia so that all other features of preeclampsia will be sought and addressed.

1. Controversy remains as to whether fetal growth restriction in the context of new-onset gestational hypertension, without any other maternal feature of preeclampsia, should be considered to define preeclampsia. The authors’ view was that this should apply given that preeclampsia, as such rises are difficult to distinguish from the usual disease.

2. Although it is probable that preeclampsia can be present in some cases without overt hypertension, ISSHP recommends maintaining new-onset hypertension in the diagnosis for now.

<table>
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<tr>
<th>Preeclampsia Superimposed on Chronic Hypertension</th>
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<tbody>
<tr>
<td>About 25% of women with chronic hypertension will develop superimposed preeclampsia. These rates may be higher in women with underlying renal disease.</td>
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<tr>
<td>This diagnosis is made when a woman with chronic essential hypertension develops any of the above maternal organ dysfunction consistent with preeclampsia.</td>
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<tr>
<td>Rises in BP per se are not sufficient to diagnose superimposed preeclampsia, as such rises are difficult to distinguish from the usual increase in BP after 20 weeks’ gestation.</td>
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<tr>
<td>In the absence of preexisting proteinuria, new-onset proteinuria in the setting of a rise in BP is sufficient to diagnose superimposed preeclampsia.</td>
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<tr>
<td>In women with proteinuric renal disease, an increase in proteinuria in the pregnancy is not sufficient per se to diagnose superimposed preeclampsia.</td>
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<tr>
<td>Diagnostic biomarkers (particularly PlGF) may assist with diagnosis and prognosis in the future but are not yet recommended for this diagnosis.</td>
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<tr>
<td>Fetal growth restriction may be part of chronic hypertension per se and cannot be used as a diagnostic criterion for superimposed preeclampsia.</td>
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Section 3. Prediction and Prevention of Preeclampsia

Predicting the Development of Preeclampsia

No first or second trimester test or set of tests can reliably predict the development of all cases of preeclampsia; however, a combination of maternal risk factors, BP, PlGF, and uterine artery Doppler can select women who may benefit in particular from 150 mg/d of aspirin to prevent preterm but not term preeclampsia. ISSHP supports first trimester screening for preeclampsia when this can be integrated into the local health system although the cost effectiveness of this approach remains to be established.

ISSHP recommends that women with established strong clinical risk factors for preeclampsia (ie, prior preeclampsia, chronic hypertension, pregestational diabetes mellitus, maternal body mass index >30 kg/m², antiphospholipid syndrome, and receipt of assisted reproduction) be treated, ideally before 16 weeks but definitely before 20 weeks, with 75 to 162 mg/d aspirin, as studied in randomized controlled trials.

Maternal characteristics and history provide strong clues to which women are more at risk of developing preeclampsia than others, particularly:

- Prior preeclampsia
- Chronic hypertension
- Multiple gestation
- Pregestational diabetes mellitus
- Maternal body mass index >30
- Antiphospholipid syndrome/SLE
- Assisted reproduction therapies

It may be possible to narrow the risk profile for preeclampsia further using a combination of these risk factors, screening of uterine artery Doppler, and plasma PlGF. This is an issue for the future.

Notes

Many clinical, ultrasonographic, and laboratory parameters have been explored during early pregnancy as tools for predicting who will later develop preeclampsia. These include, among others:

- Uterine artery Doppler studies.
- Measurement of angiogenic factors (such as soluble endoglin, PlGF; sFlt-1, and sFlt-1/PlGF ratio).
- Numerous others, such as plasma pregnancy-associated plasma protein A, placental protein 13, homocysteine, asymmetrical dimethylarginine, uric acid and leptin, urinary albumin, or calcium.

Maternal characteristics that are most strongly associated with an increased likelihood of preeclampsia include those listed above, as well as underlying renal disease or multiple pregnancies.

Other factors less strongly associated with preeclampsia include, but are not limited to:

1. Advanced maternal age.
2. Family history of preeclampsia.
3. Short duration of sexual relationship (<6 months) before the pregnancy.
4. Primiparity (although preeclampsia may occur in subsequent pregnancies even in the absence of preeclampsia in the first).
5. Primipaternity—both changed paternity and an interpregnancy interval >5 years have been associated with an increased risk for preeclampsia.
6. CKD.

7. Connective tissue diseases.
- Thrombophilias have no clear association with near-term preeclampsia, but factor V Leiden may be a risk factor for the rarer case of early onset preeclampsia, particularly when associated with severe fetal growth restriction.
- One large systematic review demonstrated that parity, preeclampsia history, race, chronic hypertension, and conception method had an area under the curve of 0.76 for predicting early onset preeclampsia and that discrimination could be improved with specialized tests. The size of the difference in area under the curve varied widely between model comparisons in this study, ranging from −0.005 to 0.24 in favor of specialized models. Improvements in discrimination were more modest for models predicting any preeclampsia and late-onset preeclampsia than for models predicting early onset preeclampsia.
- O’Gorman et al found that the detection rates for preterm and term preeclampsia were inferior using National Institute for Health and Care Excellence (NICE) or ACOG clinical criteria alone to first trimester screening using a multivariable approach (that included maternal risk factors, BP, maternal plasma pregnancy-associated plasma protein A and PlGF, and uterine artery Doppler). At a screen-positive rate of 10%, 370 women would have to be screened, and the 37 identified as being at high risk of preeclampsia treated with 150 mg/d of aspirin to prevent 1 case of preterm preeclampsia. Importantly, the vast majority (≈80%) of screen-positive women did not have strong clinical risk factors for preeclampsia.
- In the ASPRE study (Aspirin Versus Placebo in Pregnancies at High Risk for Preterm Preeclampsia), ≈27,000 women were screened, 6% were included in final analysis and 48 (≈0.2%) developed preterm preeclampsia. This type of screening added a predictive benefit for preterm preeclampsia above that of clinical predictive factors, but the cost effectiveness of the approach is not yet known. Also, screening must be undertaken clinically in the same way as in ASPRE although uterine artery Doppler (pulsatility index) is not a difficult procedure to learn.
- An important finding in the ASPRE trial was confirmation that aspirin at a dose of 150 mg at night conferred no greater risk to pregnant women (or their newborns) than placebo.
- Randomized controlled trials of rule in and rule out tests are needed and must include a coprimary non-inferiority outcome of neonatal morbidity because of the real risk of earlier delivery in these women.

Tests to Rule Out Preeclampsia

No test should be used routinely as a rule out test at this stage although PlGF testing may prove useful in selected groups in future studies. Such tests should not be used routinely in clinical practice until further clinical studies are conducted.

Notes

In May 2016, the NICE group published NICE Diagnostics guidance (DG23; (https://www.nice.org.uk/guidance/dg23) recommending that the Elecsys immunoassay for the sFlt-1/
PIGF ratio, or the Triage PIGF test, be used with standard clinical assessment to help rule out proteinuric preeclampsia or preeclampsia requiring delivery within the next 7 (for the sFlt-1/PIGF ratio) or 14 days (for Triage PIGF) in women with suspected preeclampsia between 20 and 34+6 weeks’ gestation. This recommendation was based primarily on 2 multicenter studies of women with a broad definition of suspected preeclampsia at <34+6 weeks’ gestation. The PROGNOSIS study (Prediction of Short-Term Outcome in Pregnant Women With Suspected Preeclampsia Study) found that a sFlt1/PIGF ratio <38 could reliably rule out development of preeclampsia for the next 7 days in women with a wide range of inclusion criteria; this finding may not be of any clinical advantage in centers already established for regular antenatal follow-up but may become of use in remote or low- and middle-income countries (LMIC) areas once further research is conducted. The PELICAN study (Plasma Placental Growth Factor [PIGF] in the Diagnosis of Women With Pre-eclampsia Requiring Delivery Within 14 Days) found that a Triage PIGF value of ≤100 pg/mL or the fifth centile of PIGF concentration for gestational age gave high sensitivity with good precision for identifying women likely to develop preeclampsia needing delivery within 14 days of testing, when presenting with suspected preeclampsia before 35 weeks’ gestation. PIGF, alone or in combination with sFlt-1, was not recommended to rule-in preeclampsia.

Predicting the Course of Established Preeclampsia

There are recent studies aiming to predict clinical outcomes for women when they initially present with early features of preeclampsia. Measurement of angiogenic factors may play a role in this regard in the future but is still at a research stage.56

A clinical predictive model, the PIERS model (Preeclampsia Integrated Estimate of Risk), can predict the likelihood of a composite severe adverse maternal outcome using the following variables gathered from 0 to 48 hours after admission with preeclampsia:57,58

- Gestational age
- Chest pain or dyspnea
- Oxygen saturation
- Platelet count
- Serum creatinine
- Aspartate aminotransferase

In practice, pulse oximetry is used infrequently and defaults to an oxygen saturation of 97% in the risk model when oximetry is not available (https://piers.cfri.ca/PIERSCalculatorH.aspx).

ISSHP recommends this as a useful adjunct in the initial assessment of women with preeclampsia.

Notes

The PREP Collaborative Network (Prediction of Complications in Early-Onset Preeclampsia) published prognostic models that assist predicting the overall risk of women with established preeclampsia to experience a complication using logistic regression (PREP-L) and for predicting the time to adverse maternal outcome using a survival model (PREP-S).59

The PREP-S model included maternal age, gestation, medical history, systolic BP, deep tendon reflexes, urine protein creatinine ratio, platelets, serum alanine amino transaminase, urea, creatinine, oxygen saturation, and treatment with antihypertensives or MgSO4. The PREP-L model included the above except deep tendon reflexes, serum alanine amino transaminase, and creatinine (available at http://stg.pocketapp.co.uk/qmul/#home).

Prevention

Use low-dose aspirin (preferably 150 mg/d) started before 16 weeks of pregnancy for women at increased risk for preeclampsia, particularly if any of the following conditions exist:

<table>
<thead>
<tr>
<th>Previous preeclampsia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preexisting medical conditions (including chronic hypertension, underlying renal disease, or pregestational diabetes mellitus)</td>
</tr>
<tr>
<td>Antiphospholipid antibody syndrome</td>
</tr>
<tr>
<td>Multiple pregnancy</td>
</tr>
<tr>
<td>Obesity</td>
</tr>
<tr>
<td>Assisted reproduction pregnancy</td>
</tr>
</tbody>
</table>

In the face of low calcium intake (<600 mg/d), use calcium 1.2 to 2.5 g/day in women at increased risk.

Pregnant women should exercise at least 3 days per week for an average 50 minutes using a combination of aerobic exercise, strength, and flexibility training; this has been associated with less weight gain and reduced incidence of hypertensive disorders in pregnancy; there are no significant adverse effects of exercise in pregnancy.

1. No treatment to date can prevent preeclampsia in all women.
2. In women considered to be at increased risk for preeclampsia on the basis of clinical factors mentioned above, both low-dose aspirin and calcium (in the setting of low calcium intake) are recommended for the prevention of preeclampsia.

- Aspirin should be given at a dose between 100 and 150 mg/day, started preferably before 16 weeks’ gestation, possibly taken at night, and continued until delivery: 70 women need to be treated to prevent 1 case of preeclampsia, particularly severe preeclampsia. Implementation of this practice is associated with improved outcomes;65 it is possible that initiating aspirin later than 16 weeks’ gestation may also be of benefit,66 but we recommend earlier commencement. Recent analyses question: (1) whether aspirin needs to be started before 16 weeks or still has benefit if started later, (2) the magnitude of effect (ranging from 50% to only 10% risk reduction), and (3) what dose is most beneficial, at least 100 mg seeming to be required.67-69
- The ASPRE study has demonstrated that the use of 150 mg aspirin at night in women deemed to be high risk for preterm preeclampsia on the basis of screening with maternal factors, and Doppler and maternal PIGF reduced the incidence of preterm preeclampsia from 4.3% to 1.6% in the aspirin group.37
- Enoxaparin does not offer any preventative advantage above low-dose aspirin even in women at high risk for preeclampsia.70
3. Calcium at a dose of at least 1 g/d has been shown to reduce the likelihood of preeclampsia in women with low calcium intake. The CAP trial (Calcium and Pre-eclampsia) data will be further reported to examine preventative benefits.
of supplemental calcium in women who are calcium replete (after prepregnancy and early pregnancy replacement of 500 mg/d) compared with women who are not replete. This may change future recommendations.

4. Exercise using an ACOG program guideline (or aerobic exercise for 50 minutes, 3× per week) in 1 randomized controlled trial of 765 women has been associated with reduced gestational hypertension and preeclampsia, as well as less weight gain and macrosomia.72

5. Supplemental vitamin C and E are not recommended and may in fact be associated with worse pregnancy outcomes.73

**Fetal Monitoring and Management for the Hypertensive Disorders of Pregnancy**

Fetal biometry (biparietal diameter together with head circumference, abdominal circumference, and femur length which are computed to produce an estimate of fetal weight), amniotic fluid volume assessment, and fetal Doppler waveform analysis should be performed at the first diagnosis of preeclampsia.

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>In confirmed preeclampsia or where there is fetal growth restriction</td>
<td>Serial evaluation of fetal growth, amniotic fluid volume, and UA Doppler are recommended from 24 weeks’ gestation until birth, with fetal growth evaluated no more frequently than at 2 weekly intervals. Advice should always be sought about ultrasound testing from maternal fetal medicine specialists for earlier gestation cases.</td>
</tr>
<tr>
<td>More frequent ultrasound measurements are needed if there is high UA resistance or absent or reversed end-diastolic flow; in these cases, specialized opinion must be sought.</td>
<td></td>
</tr>
<tr>
<td>Prenatal corticosteroids for fetal lung maturation should be given between 24+0 and 34+0 weeks gestation but may be given up until 38+0 weeks in cases of elective delivery by caesarean section; multiple steroid courses are not recommended.</td>
<td></td>
</tr>
<tr>
<td>MgSO4 for fetal neuroprotection should be administered in gestations before 32 weeks.</td>
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</tr>
</tbody>
</table>

**Notes**

Preeclampsia is, at least in part, a disease of placenta/placental dysfunction and the fetus is potentially vulnerable to the effects of uteroplacental insufficiency, particularly fetal growth restriction and placental abruption.

1. In addition to the ideal schedule of a first trimester dating ultrasound and a midtrimester anomaly scan, fetal biometry, amniotic fluid volume assessment, and fetal Doppler waveform analysis should be performed at the first diagnosis of preeclampsia.

2. The ideal scanning schedule thereafter is determined by the presence (or absence) of fetal growth restriction at the initial assessment and the gestation at diagnosis.

   - The ACOG and Royal College of Obstetricians and Gynecologists (https://www.rcog.org.uk/en/guidelines-research-services/guidelines/gtg31/) agree that the risk of perinatal morbidity and mortality increases once the estimated fetal weight or the abdominal circumference <10th centile.

   - ACOG considers amniotic fluid an important diagnostic and prognostic parameter in fetuses with intrauterine growth restriction, whereas the Royal College of Obstetricians and Gynecologists notes that amniotic fluid assessment has minimal value in diagnosing growth restriction. Both guidelines agree that UA Doppler is not a reliable screening technique for fetal growth restriction but is a useful assessment tool once fetal growth restriction is diagnosed.

   - The Society of Obstetricians and Gynecologists of Canada74 uses an estimated fetal weight <10th centile for diagnosis of small for gestational age and suggests that UA and uterine artery Doppler studies in combination with ultrasound of the placental morphology are useful to establish a more refined diagnosis of fetal growth restriction.

3. In confirmed preeclampsia, where the maternal condition allows for continuation of pregnancy, serial evaluation of fetal growth, amniotic fluid volume, and UA Doppler are recommended from 26 weeks’ gestation until birth.

4. The fetal biometry should be assessed no more frequently than every 2 weeks.

5. Criteria for the diagnosis of fetal growth restriction include an estimated fetal weight <10th centile on ultrasound based on accurate dating. In particular, an estimated fetal weight <third centile and abnormal UA Doppler significantly increase the risk of adverse perinatal outcome.

6. Once fetal growth restriction is diagnosed, assessment of fetal growth is recommended at 2 weekly intervals. In addition, amniotic fluid volume and UA Doppler assessment should be performed.

7. If the UA Doppler demonstrates increased resistance (pulsatility index >95th centile), the sonographic surveillance should be increased to weekly intervals or more frequently if deemed necessary by the managing clinician.

8. If there is absent end-diastolic flow in the UA before 34 weeks’ gestation, daily cardiotocograph monitoring, twice weekly UA Doppler, and amniotic fluid volume assessment are recommended. These women should be discussed with the team consultant on a daily basis.

9. If there is reversed end-diastolic flow in the UA before 30 weeks gestation, admission to hospital with daily cardiotocograph monitoring, 3× weekly UA Doppler, and amniotic fluid volume assessment are recommended; an opinion from a fetal medicine specialist may be sought to determine fetal viability and guide further management.

10. In cases of absent end-diastolic flow, delivery should be considered no later than 34 weeks gestation. Earlier delivery may be indicated in cases of poor interval growth or a deterioration of sonographic variables (Doppler, amniotic fluid).

11. In cases of reversed end-diastolic flow, delivery should be considered no later than 30 weeks gestation. Earlier delivery may be indicated by a deterioration of sonographic variables.

12. Prenatal corticosteroids for fetal lung maturation should be considered between 24+0 and 34+0 weeks gestation but may be given up until 38+0 weeks in cases of elective delivery by caesarean section. Steroids should be administered in a timed manner. Multiple courses of steroids are not recommended.

13. Decisions on the optimal timing of delivery need to be made on an individual basis and may require the involvement of an experienced obstetrician or fetal medicine specialist, in particular in severe, preterm fetal growth restriction.

14. MgSO4 for fetal neuroprotection should be administered if delivery is planned before 32 weeks gestation.

15. Mode of delivery needs to be discussed on an individual basis, but caesarean section is likely when absent or reversed end-diastolic flow UA Doppler waveforms are present, or in very preterm gestations.
16. If induction of labor is considered in women with abnormal UA Doppler, a continuous cardiotocograph should be performed once contractions have started, with a low threshold for caesarean delivery.

17. Cord arterial and venous pH should be recorded for all fetal growth restricted infants.

18. Histopathologic examination of the placenta is strongly recommended in all cases where fetal growth restriction is diagnosed prenatally or at birth to understand the underlying causes and guide management in a subsequent pregnancy.

Section 4. Management Principles for the Hypertensive Disorders of Pregnancy

Chronic Essential Hypertension

Use antihypertensives to maintain BP in the range 110 to 140/80 to 85 mm Hg.

Acceptable initial antihypertensives include labetalol, oxprenolol, methyldopa, nifedipine, diltiazem; prazosin and hydralazine are usually used as second or third line agents.

Home BP monitoring is a useful adjunct to clinic visits if available; ≈¾ home BP devices are accurate, so we recommend checking device accuracy against a sphygmomanometer for each woman.

The key risks of chronic essential hypertension are as follows:
- Superimposed preeclampsia
- Fetal growth restriction
- Accelerated maternal hypertension

Therefore, monitor for developing preeclampsia using urinalysis at each visit along with clinical assessment and blood tests (Hb, platelet count, liver transaminases, uric acid, and creatinine) at 28 and 34 weeks as a minimum.

Assess fetal well-being with ultrasound from 26 weeks’ gestation and thereafter at 2 to 4 weekly intervals if fetal biometry is normal and more frequently in the presence of suspected fetal growth restriction (see above).

Indications for delivery are similar to those of preeclampsia (see below); if no such indication arises, delivery at 39 weeks seems optimum.

Notes
1. The CHIPS trial (Control of Hypertension in Pregnancy Study) enrolled mostly chronic hypertensive women; targeting a diastolic BP of 85 mm Hg was associated with reduced likelihood of developing accelerated maternal hypertension and no demonstrable adverse outcome for babies compared with targeting higher diastolic BP. Therefore, current evidence supports controlling BP to these levels.

Chronic Hypertension Because of Renal Disease

Management of this group is complex and beyond the scope of this document but is discussed in detail elsewhere. General principles include:

- Maternal and fetal outcomes are generally worse than the general population even when CKD is mild.
- Control of maternal BP is important to pregnancy and long-term maternal renal outcome.
- Monitoring for superimposed preeclampsia and for adequate fetal growth is important.
- Early dialysis with an aggressive dialysis prescription of ≈36 hours per week seems to convey the best outcome for those with progressive renal disease in pregnancy.

White-Coat Hypertension

Where a diagnosis of white-coat hypertension is confirmed, pregnant women can be managed with regular home BP assessments and antihypertensives can be avoided, at least up to office BP levels of 160/110 mm Hg.

There are limited studies on the outcome of these pregnancies, but it seems that up to half will develop true gestational hypertension or preeclampsia; it is possible that the risk of preeclampsia is twice that of the normal pregnant population although this needs to be confirmed. The important messages around white-coat hypertension are as follows:
- It is reasonable to withhold antihypertensive therapy in this group.
- BP should continue to be monitored regularly at home.
- Increased surveillance is required throughout pregnancy to detect the emergence of preeclampsia.

In areas where home BP assessments are not available, maternal BP should be checked regularly, preferably weekly, by a healthcare worker; this is probably best done by someone other than a doctor to reduce the likelihood of a white-coat effect (Figure 1).

Gestational Hypertension

The Key Principles of Management of Gestational Hypertension

Control BP to levels of 110 to 140/85 mm Hg, as above.

Monitor for development of preeclampsia.

Monitor fetal growth, especially if maternal uric acid is elevated.

Delivery can be delayed until 39+6 weeks provided BP can be controlled, fetal monitoring is reassuring, and preeclampsia has not developed.

Notes
1. The CHIPS trial (Control of Hypertension in Pregnancy Study) enrolled mostly chronic hypertensive women; targeting a diastolic BP of 85 mm Hg was associated with reduced likelihood of developing accelerated maternal hypertension and no demonstrable adverse outcome for babies compared with targeting higher diastolic BP. Therefore, current evidence supports controlling BP to these levels.
Notes

1. By definition, gestational hypertension is not a benign disorder as at least a quarter of such cases will progress to become preeclampsia.\(^2\)
2. There is no specific test or set of tests that allow prediction of which women with gestational hypertension will develop preeclampsia at the time they are diagnosed with gestational hypertension although the risk is highest among those who present with gestational hypertension at <34 weeks.\(^2\)
3. Women with gestational hypertension require assessment in hospital if they develop preeclampsia or severe hypertension ≥160/110 mm Hg.
4. The optimum time for delivery remains uncertain for women with gestational hypertension and no features of preeclampsia. A large retrospective study concluded an optimum time of 38 to 39 weeks,\(^4\) but this will need to be clarified with future randomized trials.

Preeclampsia

Antenatal

ISSHP endorses the following key management points:

Regardless of the hypertensive disorder of pregnancy, BP requires urgent treatment in a monitored setting when ≥160/110 mm Hg; acceptable agents for this include oral nifedipine or intravenous labetalol or hydralazine.

Regardless of the hypertensive disorder of pregnancy, we recommend that BPs consistently at or ≥140/90 mm Hg be treated aiming for a target diastolic BP of 85 mm Hg and systolic BP at least ≤160 mm Hg; some units target 110–140 mm Hg to reduce the likelihood of developing severe maternal hypertension and possibly other complications, such as low platelets and elevated liver enzymes with symptoms. Antihypertensive drugs should be reduced or ceased if diastolic BP falls <80 mm Hg. Acceptable agents include oral methyl dopa, labetalol, oxprenolol, nifedipine, with second or third line agents hydralazine and prazosin.

Women with preeclampsia should all be assessed in hospital when first diagnosed; thereafter, some may be managed as outpatients once it is established that their condition is stable and they can be relied on to report problems and monitor their BP.

Women with preeclampsia who have proteinuria and severe hypertension, or hypertension with neurological signs or symptoms, should receive MgSO\(_4\) for convulsion prophylaxis.

Plasma volume expansion is not recommended routinely in women with preeclampsia.

Fetal monitoring in preeclampsia should include assessment of fetal biometry, amniotic fluid, and UA Doppler with ultrasound at first diagnosis and thereafter at 2 weekly intervals if the initial assessment was normal and more frequent amniotic fluid and Doppler in the presence of fetal growth restriction.

Maternal monitoring in preeclampsia should include BP monitoring, repeated assessments for proteinuria if not already present, clinical assessment including clonus, and twice weekly blood tests for Hb, platelet count, liver transaminases, creatinine, and uric acid. Blood test evaluation should be performed at least twice weekly (and again in response to a change in clinical status) in most women with preeclampsia.

There should be no attempt to diagnose mild versus severe preeclampsia clinically as all cases may become emergencies, often rapidly.

Women with preeclampsia should be delivered if they have reached 37 weeks' gestation or they develop any of the following: repeated episodes of severe hypertension despite maintenance treatment with 3 classes of antihypertensive agents; progressive thrombocytopenia; progressively abnormal renal or liver enzyme tests; pulmonary edema; abnormal neurological features, such as severe intractable headache, repeated visual scotomata, or convulsions; or nonreassuring fetal status. Neither the serum uric acid nor the level of proteinuria should be used as an indication for delivery.

In low resource settings, all women with preeclampsia should receive MgSO\(_4\) for convulsion prophylaxis, typically a loading dose of 4 g IV or 10 g IM, followed by 5 g IM every 4 hours or an infusion of 1 g/h until delivery and for at least 24 hours postpartum.

In other centers, women should receive MgSO\(_4\) if they have severe hypertension (≥160/110 mm Hg) and proteinuria or if there are premonitory signs of eclampsia, such as severe headaches, repeated visual scotomata, or clonus.

ISSHP does not advocate for any clinical distinction between mild and severe preeclampsia in usual clinical practice. Instead, all cases of preeclampsia should be treated in the knowledge that the condition can change rapidly and that worldwide, this remains a major cause of maternal mortality.

Delivery should be effected depending on gestational age and maternal and fetal status, as follows:

- Women with onset of preeclampsia at ≥37 weeks’ gestation should be delivered.
- Women with onset of preeclampsia between 34 and 37 weeks’ gestation should be managed with an expectant conservative approach, as below.
- Women with onset of preeclampsia at <34 weeks’ gestation should be managed with a conservative (expectant) approach at a center with Maternal and Fetal Medicine expertise.
- Women with preeclampsia with a fetus at the limits of viability (generally before 24 weeks gestation) should be counseled that termination of pregnancy may be required.

Delivery is necessary when ≥1 of the following indications emerge:

- Inability to control maternal BP despite using ≥3 classes of antihypertensives in appropriate doses
- Maternal pulse oximetry <90%
- Progressive deterioration in liver function, creatinine, hemolysis, or platelet count
- Ongoing neurological features, such as severe intractable headache, repeated visual scotomata, or eclampsia
- Placental abruption
- Reversed end-diastolic flow in the UA Doppler velocimetry, a nonreassuring cardiotocograph, or stillbirth

Notes

1. The level of BP itself is not a reliable way to stratify immediate risk in preeclampsia because some women may develop serious organ dysfunction, such as renal impairment or neurological complications, at relatively mild levels of hypertension. Hence, decisions to admit and monitor should be based on having developed preeclampsia regardless of the initial BP levels.
2. BP at or ≥160/110 mm Hg are thought to be surrogate markers for the risk of stroke, as well as a reflection...
of increased severity of the overall condition of pre-eclampsia. In the follow-up of women in the CHIPS trial, the development of severe hypertension was associated with significantly greater likelihood of adverse outcomes for both the baby (ie, low birth weight, prematurity, death, and morbidity requiring neonatal unit care) and the mother (ie, thrombocytopenia, abnormal liver enzymes with symptoms, and longer hospital stay). Among women who were managed at the higher BP target (of less tight control), severe hypertension was also associated with significantly more serious maternal complications.

3. There is no universal agreement in clinical practice guidelines as to what BP level should be maintained when antihypertensives are instituted for nonurgent indications in pregnancy. However, all guidelines were published before publication of the CHIPS Trial results. The Canadian guidelines recommend 130 to 155/90 to 105 mmHg in the absence of comorbid conditions, and the NICE guidelines recommend keeping BP <150 mmHg systolic and between 80 and 100 mmHg diastolic. The USA Society for Maternal-Fetal Medicine decided not to endorse the finding of the CHIPS trial. Yet, as pointed out editorially to manage BP expectantly at <160/110 mmHg but emergently at ≥160/110 mmHg is logically inconsistent. ISSHP endorses an approach that seeks to reduce the likelihood of developing severe maternal hypertension, namely commencing antihypertensives to treat any persistent nonsevere hypertension, well before BPs of 160/110 mmHg are reached. This recommendation applies to all hypertensive disorders of pregnancy. CHIPS enrolled women with chronic (75%) or gestational (25%) hypertension, but superimposed preeclampsia developed in almost half of women, and they continued to receive the BP treatment to which they were randomized for 2 subsequent weeks before delivery.

4. The target BP for antihypertensive therapy in the tight control arm of CHIPS was a diastolic BP of 85 mmHg and a systolic BP <160 mmHg. Each unit should have a protocol (based on national or international recommendations) that documents their recommended target BP and regular audit of associated pregnancy outcomes is recommended.

6. There is clear evidence that MgSO4 prevents eclampsia, approximately halving the rate; overall ~100 women need MgSO4 to prevent 1 seizure. ISSHP recommends that especially because the cost benefit is greatest, all preeclamptic women in LMICs should receive MgSO4. In highly specialized centers, and in high-income settings where the costs of administering MgSO4 are higher, selective use in women with preeclampsia is reasonable. In the landmark MAGPIE trial (Magnesium Sulphate for Prevention of Eclampsia), women with preeclampsia were given MgSO4 if they had severe hypertension and at least 3+ of proteinuria or slightly lower measurements (150/100 mmHg and at least 2+ of proteinuria) in the presence of at least 2 signs or symptoms of imminent eclampsia (which was not defined but is taken to mean headache, visual symptoms, or clonus). ISSHP recommends that each unit has a consistent policy on their use of MgSO4 that incorporates appropriate monitoring, recognition of the risks of MgSO4 infusions, and assessment of maternal and fetal outcomes. The dosing regimens used in the Eclampsia and MAGPIE trials should be used.

7. The duration of MgSO4 use postpartum remains contentious; one recent study in Latin America found that women who had received at least 8 g of MgSO4 before delivery had no additional benefit of continuing the magnesium for a further 24 hours postpartum. This approach needs to take into consideration the known incidence of eclampsia postpartum. As such, either approach is reasonable, but until further studies confirm these findings in other populations, we recommend continuing MgSO4 for 24 hours postpartum. Each unit should develop their own protocols for postpartum magnesium.

### Intrapartum

- **Oral antihypertensives should be given at the start of labor.**
  - Treat hypertension urgently with oral nifedipine or either intravenous labetalol or hydralazine if BP rises ≥160/110 mmHg.
  - Total fluid intake should be limited to 60 to 80 mL/h.

### Notes

1. Reduced gastrointestinal motility may decrease absorption of antihypertensives after oral administration. Therefore, intravenous antihypertensives may be needed to control BP, particularly if it becomes severe.

2. Fluid balance should aim for euvolemia as at all other times. Preeclamptic women have capillary leak but may have either reduced or increased cardiac output. To ensure euvolemia, insensible losses should be replaced (30 mL/h) along with anticipated urinary losses (0.5–1 mL/kg per hour). We suggest using 60–80 mL/h to avoid risks of pulmonary edema. There is no rationale to “run dry” a preeclamptic woman as she is already at risk of AKI.

### Postpartum

- Monitor BP at least 4 to 6 hourly during the day for at least 3 days postpartum.
  - Preeclampsia may develop de novo intra- or early postpartum; such cases should be managed as above and a careful assessment for retained products should be made; these cases often take longer to settle postpartum.
  - Monitor general well-being and neurological status as per predelivery; eclampsia may occur postpartum.
  - Repeat Hb, platelets, creatinine, liver transaminases the day after delivery and then second daily until stable if any of these were abnormal before delivery.
  - Antihypertensives should be restarted after delivery and tapered slowly only after days 3 to 6 postpartum unless BP becomes low (<110/70 mmHg) or the woman becomes symptomatic in the meantime.
  - Most women can be discharged by day 5 postpartum, especially when they are able to monitor their BP at home.
  - Avoid NSAIDs in women with preeclampsia if possible, especially in the setting of AKI, and use alternative pain relief.
Long-Term Follow-Up

Women with preeclampsia should be reviewed within 1 week if still requiring antihypertensives at discharge from hospital.

All women should be reviewed 3 months postpartum by which time BP, urinalysis, and all laboratory tests should have normalized.

Further investigation is required for persistent abnormalities, including a work-up for secondary causes of persistent severe hypertension or underlying renal disease with persistent proteinuria.

Assessment should also include a clinical check for depression, anxiety, or posttraumatic stress disorder symptoms.101

Long-Term Follow-Up

All women with chronic hypertension, gestational hypertension, or preeclampsia require lifelong follow-up because of their increased cardiovascular risk. We recommend:

Advice to women with gestational hypertension or preeclampsia that they have increased risks of cardiovascular disease, death, stroke, diabetes mellitus, venous thromboembolic disease, and CKD compared with women who have had normotensive pregnancies.104

Advice to women with preeclampsia that they have an approximately 15% risk for developing preeclampsia again and a further 15% risk for gestational hypertension in a future pregnancy102,103 and that they should receive low-dose aspirin in another pregnancy.

Advice to women with gestational hypertension that they have approximately a 4% risk for developing preeclampsia and a further 25% risk for gestational hypertension in a future pregnancy.105,106

Advice to women with gestational hypertension or preeclampsia that they have increased risks of small for gestational age babies in another pregnancy even if preeclampsia does not recur.

Regular follow-up with a general practitioner to monitor BP and periodic measurement of fasting lipids and blood sugar.

Adopt healthy lifestyle with maintenance of ideal weight and regular aerobic exercise.

Notes

1. There is controversy as to whether NSAIDs are harmful or not in this setting. Certainly, some women develop severe hypertension from NSAIDs,98 but other observational studies suggest that the risk is small, if any.99,100 NSAIDs are effective analgesics. Until prospective randomized trials are conducted on this issue, we recommend using alternative analgesia as a first choice for women who have preeclampsia.

2. It is probable that in the long-term these women have some degree of underlying metabolic syndrome and higher BP than women who did not have hypertensive pregnancies.107

3. The values we use to define normal BP are derived from older and often male populations; ongoing studies will define a new normal range of BP for young women who have not had preeclampsia, thereby permitting a reassessment of whether a woman who has had preeclampsia truly has normal BP when followed up 6 months or more postpartum.110

4. Even with an elevated lifetime risk of cardiovascular disease, young women may have low 10-year cardiovascular risk scores using well-established tools and may be overlooked as being at high risk on that basis.

5. Ongoing clinical studies may provide more specific information on how best to manage formerly preeclamptic women.

Section 5. Application of These ISSHP Recommendations to Low Resource Countries

General Recommendations

1. The recommendations described in this document are for an ideal setting. In some instances, it may not be possible to adopt all of these recommendations. Health systems in LMICs may have to consider the minimum required to reach as many women as possible.

2. It is recommended that there is ongoing review and update of national and facility clinical guidelines, preservice educational material, and in-service training materials to ensure that all documents reflect these ISSHP recommendations so as to improve outcomes for women and babies.

3. In circumstances where the documented goals of this guideline are not attainable in their entirety, physicians should work pragmatically toward them as far as the local resources allow.

4. It is the responsibility of managing physicians to advocate for the use of effective interventions whether they practice in well- or under-resourced settings.

5. The distances between community clinics and referral hospitals are often large, and transport problems exist. For this reason, patients diagnosed with preeclampsia should be referred as soon as possible to a center with an appropriate level of care and managed as inpatients.

6. The effectiveness of referral systems in many LMIC is less than optimal, and many rural areas are without centers that can provide basic obstetric and neonatal services. Women diagnosed with preeclampsia in such settings should be advised to relocate immediately to areas with better healthcare services, especially where they have family members if possible.

7. Communities should put strategies in place for transport from clinics or primary healthcare centers to referral centers.

8. All healthcare facilities should regularly review and update facility and community health worker referral pathways for women with preeclampsia.

9. All women with a hypertensive disorder of pregnancy require delivery in a center that provides emergency obstetric and neonatal care while women with maternal complications require delivery in a center capable of providing maternal critical care. Those with pregnancies at the limit of viability require the highest available level of neonatal support.

10. Antihypertensive agents for treatment of moderate and severe hypertension and MgSO4 to prevent or treat eclampsia must be available at community level centers and clinics so that patients can be stabilized and referred safely.

11. Women with preeclampsia in LMICs may have a limited comprehension of the nature and risks of the disease. A
South African study showed that a structured information sheet (in addition to verbal counseling by a physician) improved patients’ understanding and knowledge in a limited way but did not alleviate their anxiety. Better understanding of the disease will lead to greater acceptance of advantageous treatment options and prime the patient for life-long care of her health.

12. A key issue is the supply of MgSO₄ which is rarely in stock; there are challenges with out of stock, challenges with the distribution system, the drug often being stuck at district level, and then sitting there without getting to the healthcare facility. Priority should be given to provision of such stock.

Antenatal Care
The 2016 World Health Organization guidelines on routine antenatal care (ANC) (http://www.who.int/reproductivehealth/publications/maternal_perinatal_health/anc-positive-pregnancy-experience/en/) recommends several health systems interventions to increase use of antenatal services and improve the quality of care delivered. Recommendations include

- Midwife-led continuity of care throughout the antenatal, intrapartum, and postnatal periods;
- A minimum of 8 ANC contacts;
- Women-held case notes;
- Promotion of health-related behaviors and distribution of nutrition supplements;
- Recruitment and retention of health workers in rural and remote areas (where 1 of 20 people do not have access to essential health services); and
- Community mobilization to improve communication and support to pregnant women.

Prevention of Hypertensive Disorders in Pregnancy

<table>
<thead>
<tr>
<th>Preventive Intervention</th>
<th>Target Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prophylactic use of aspirin</td>
<td>One or more of the major risk factors for preeclampsia (Prior preeclampsia, chronic hypertension, gestational diabetes mellitus, maternal body mass index &gt;30, CKD, antiphospholipid syndrome)</td>
</tr>
<tr>
<td>or ≥2 of minor risk factors</td>
<td>(Advanced maternal age, family history of preeclampsia, short duration of sexual relationship [&lt;6 months] before the pregnancy, primiparity, primipaternity—both changed parity and an interval &gt;5 years have been associated with an increased risk for preeclampsia, connective tissue disorders)</td>
</tr>
<tr>
<td>Preferably starting before 16 weeks’ gestation, until 37 weeks, using 100 to 150 mg daily</td>
<td>Calcium supplements 1200 mg daily if dietary calcium intake is low in the local population</td>
</tr>
</tbody>
</table>

Notes

1. Knowledge of prophylactic use of aspirin, and calcium where dietary intake is low, is poor in district and health centers, even among doctors (Landscape analyses in Nigeria and Bangladesh—Ending Eclampsia—Population Council www.endingeclampsia.org).

Early Detection and Diagnosis

1. The main challenge is to identify women at risk of developing preeclampsia to receive aspirin and calcium supplementation before 16 weeks. Women in LMIC do not usually seek care much before 20 weeks. Therefore, community-based messaging and education is required.

2. There is a need to ensure time and counseling skills in order that women take aspirin and calcium:
   - Confirm aspirin and calcium dosing and timing as per these international recommendations.
   - Ensure aspirin prophylaxis is included in all national guidelines and protocols.
   - Consider group-based counseling and task shifting so that lower level healthcare workers can provide aspirin and calcium to women in areas where there is known calcium deficiency or a high prevalence of preeclampsia and for women with risk factors for preeclampsia as above.

3. Antiphospholipid antibody syndrome is not commonly diagnosed in LMIC or routinely seen as a risk factor; in any case enoxaparin is not widely available.

4. Health managers and facilities must estimate the expected number of pregnancies per annum and budget and procure aspirin and calcium in a timely manner to prevent stock-outs and thereby ensure women benefit from these simple preventative measures.

Notes

1. Clear protocols are required in each unit, utilizing the ISSHP recommendations for diagnosis and management.

2. Confusion remains on definitions of hypertension and knowledge gaps persist across providers at both secondary and primary facilities, including when to initiate antihypertensives. These ISSHP recommendations should be publicized across LMIC as the standards to be sought.

3. In LMIC settings, home BP monitoring is unlikely. Women should be encouraged to attend for a minimum of 8 ANC visits and attend more frequently if they develop warning symptoms or signs of preeclampsia or BP was raised on prior visits. They must know their BP numbers and understand the importance of knowing what their BP should be, both before and after delivery. This requires ongoing education aiming toward women understanding the significance of having a raised BP.
4. In LMIC settings, visual dipstick for proteinuria is used, not automated measurement. Often because of resource constraints, dipstick is only done if BP is raised (>140/90 mm Hg). It is important for local groups to lobby for consistent supply.

5. The gold standard continues to be the 24-hour urine protein measurement in LMIC. Quantifying with spot urine protein/creatinine ratio is rarely available, but efforts should be made to ensure urine creatinine measurement is available, thereby enabling spot PCR to be done. This should be a priority given the challenges and potentially dangerous time delays inherent in doing 24 hours urine collections. Although it is unlikely to be done at primary healthcare level, health providers should work to ensure this is available in the tertiary hospital setting.

6. Women in LMICs are usually referred to tertiary hospitals to receive all tests. However, many women do not go because of costs related to transport and to treatment. A signs- and symptoms-based model (miniPIERS) is available to identify women at low risk of complications, and this should be explored for use at primary and secondary care levels.

### Fetal Monitoring

In some LMICs in tertiary facilities, first and midtrimester ultrasound, fetal biometry, amniotic fluid volume, and fetal Doppler studies take place. Fundal height measurements may also take place every 2 weeks. However, the recent World Health Organization ANC guidelines suggest that the following should not be continued because of insufficient evidence:

1. Routine daily fetal movement counting
2. Symphysis-fundal height measurement
3. Routine antenatal cardiotocography
4. Although recommended before 24 weeks, ultrasound should only be performed where capacity exists; Units should consider costs and maintenance of ultrasound equipment over the cost of ensuring sphygmomanometers are widely available to measure BP, which can provide greater recognition of women with preeclampsia.

### Management of Hypertensive Disorders of Pregnancy

<table>
<thead>
<tr>
<th>Aims</th>
<th>Target</th>
<th>Act</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aim to maintain BP 110 to 140 /85 mm Hg.</td>
<td>Typically, methyldopa and nifedipine are used and both are acceptable.</td>
<td>Women with preeclampsia should all be assessed in hospital when first diagnosed; thereafter, some may be managed as outpatients once it is established that their condition is stable and they can be relied on to report problems and monitor their BP.</td>
<td>Laboratory tests are not always available at primary- or even secondary-level health facilities; when transfer to a higher level of care is not available, clinical decisions must be made using BP measures, fundal height assessment, symptoms, and urine dipstick testing when available.</td>
</tr>
<tr>
<td>At first referral level, antihypertensive therapy and MgSO4 should be adjusted or continued as appropriate, and women should be triaged for appropriate referral to tertiary-level care, including those eligible for expectant care and those at high risk of or with severe maternal morbidity.</td>
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</tbody>
</table>

One protocol for treatment of acute severe hypertension is described in Figure 2; others may be developed by individual units as desired.

| Treatment and prevention of eclampsia is achieved ideally with the protocol of intravenous magnesium (Figure 3), which is that used in the MAGPIE trial; when this is not possible, the Pritchard regimen (also used in the MAGPIE trial) can be used as follows: |
| Four gram is administered as an intravenous dose and 5 g in one buttock and another 5 g in the other buttock. These together constitute the loading dose (14 g). Thereafter, 5 g is administered every 4 hours for 24 hours in alternate buttocks as maintenance dose. |
| At gestational age <34 weeks, repeatedly weigh the relative benefits and risks of continuation of pregnancy against progression of maternal disease, using the recommendations for timing of delivery in this document, viz: |
| Repeated episodes of severe hypertension despite maintenance treatment with 3 classes of antihypertensive agents |
| Progressive thrombocytopenia |
| Progressively abnormal renal or liver enzyme tests |
| Pulmonary edema |
| Abnormal neurological features, such as severe intractable headache, repeated visual scotomata, or convulsions |
| Nonreassuring fetal status |
| Prenatal corticosteroids for fetal lung maturation should be given between 24+0 and 34+0 weeks gestation but may be given up until 38+0 weeks in cases of elective delivery by caesarean section; multiple steroid courses are not recommended. |

### Notes

1. Task-shifting guidelines for both MgSO4 and antihypertensive treatment should be available in each unit so that lower level providers can initiate treatment with a loading dose and refer.
   • Task-shifting policies vary on whether lower level providers can prescribe antihypertensives to keep BP in the range 110 to 140/85 mm Hg. A change in practice should be explored so that asymptomatic women without proteinuria or other evidence of preeclampsia could receive antihypertensives from lower level providers.
   • Task-shifting policies may only allow administration of intramuscular MgSO4. In such cases, a woman should receive a loading dose of IM 5 mg MgSO4 in each buttock and refer. It is better to initiate treatment with this dose than refer without any MgSO4.

2. Clear protocols are required in each unit, utilizing these ISSHP recommendations.

3. In LMIC, oxprenolol, diltiazem, and prazosin are not readily available and are costly; methyldopa and nifedipine are more readily available and either can be used as a first-line treatment.

4. Regular blood work-up at 28 and 34 weeks may not happen if a woman is not near a tertiary facility. Ultrasound is also not always available. Mostly, workers use serial fundal height check.

5. Ensure every health facility/unit has clear clinical protocols for MgSO4 use; this is a key education priority. One study demonstrated that use of MgSO4 for prevention and treatment of eclampsia varied widely and was largely inconsistent with current international guidelines.
6. There is often poor knowledge of how to monitor for MgSO₄ toxicity; this is a key area for education; the protocols in Figure 3. can be used.

**Chronic Hypertension in Pregnancy**

In LMIC, oxprenolol, diltiazem, and prazosin are not readily available and costly; methyldopa and nifedipine are more readily available and either can be used as a first line treatment.

Where resources are limited and the combination of chronic hypertension and obesity are prevalent, the recommended tests may be reduced to hemoglobin, platelet count, serum creatinine, urinalysis, and appropriate quantification of urinary protein as baseline reference.

Community-based BP measurement and protein dipsticks should be made available for women at first point of care—either by community-based health worker or at primary healthcare level living far from tertiary/hospitals facilities.

Task-shifting policies vary on whether lower level providers can prescribe antihypertensives to keep BP in the range 110 to 140/85 mm Hg. A change in practice should be explored so that asymptomatic women with chronic hypertension without evidence of preeclampsia could receive antihypertensives from lower level providers on an outpatient basis.

**Postnatal Care**

Blood pressure should be recorded shortly after birth and if normal again within 6 hours.

Postnatal BP should be controlled as per ISSHP recommendations.

In LMIC, blood tests are usually done twice in the week after birth if abnormal before delivery.

All women should have BP recorded and defer discharge for at least 24 hours or until vital signs are normal and treated or referred. Any woman with an obstetric complication and newborn with complications should stay in the hospital until both are stable.

World Health Organization recommendations include

Stay in the facility for at least 24 hours.

Check up within 48 to 72 hours of the birth and again at 7 to 14 days and at 6 weeks postpartum. A home visit within the first week is recommended for those who did not deliver in a health facility.

All women should be reminded of the danger signs of preeclampsia after birth, including headaches, visual disturbances, nausea, vomiting, epigastric or hypochondrial pain, feeling faint, or convulsions.
1. Discharge and follow-up should occur at tertiary facility; referral to a physician at hospital is advised if hypertensive or renal problems persist. Every woman should have details/documents to provide to the primary healthcare facility for close follow-up.

2. It is important to counsel/provide education on postpartum contraception and family planning about limiting/spacing of next pregnancy. Family planning counseling should start in the ANC and be offered to each woman before she leaves the facility and again when advised to come back at 6 weeks for infant immunization and family planning consultation. Any family planning method that the woman wants to receive is acceptable if based on comprehensive counseling (and is available in the particular country setting).

3. In many LMIC, women go home within 6 to 24 hours after birth. This should be discouraged after a preeclamptic pregnancy. Even in busy units with heavy pressure on postnatal beds, women with preeclampsia should not be discharged early.

4. It is an important opportunity at the time of discharge to reinforce the importance of early ANC in the next pregnancy because of risks of recurrent preeclampsia.

What Do Other Guidelines Say?
ISSHP acknowledges the expertise and rigorous approach that has been undertaken in the development of several key guidelines including:

1. NICE 2010
2. SOMANZ (Society of Obstetric Medicine of Australia and New Zealand) 2014
3. Canadian 2014
4. ACOG 2013

The key areas in which these guidelines differ are as follows:

1. The requirement for proteinuria in the diagnosis of preeclampsia (NICE).
2. The level at which routine antihypertensive treatment of BP is mandatory and the target BP thereafter (although all were published before the CHIPS Trial results were available).
3. When MgSO4 should be administered.

Other guidelines include those of World Health Organization 2011 and the Integrated Management of Pregnancy and Childbirth 2017. Adopting the management recommendations of any of these guidelines is entirely justified although one aim of the ISSHP is to see a single set of flexible and regularly updated guidelines throughout the world so as to reduce confusion around diagnosis and management of women with hypertension in pregnancy.

Importantly, ISSHP recommends that each unit has a specific policy as to management guidelines that are to be followed so that there is uniform practice within each unit. In addition, each unit should strive to record and evaluate their maternal and fetal outcomes to ensure that their policies and guidelines remain appropriate at all times.

Guideline Process
The first author drafted the initial document and sought further input from all coauthors; these authors were chosen as being expert members of the ISSHP executive (authors 1–7) with additional authors who had expertise and experience in the management of preeclampsia in low resource countries (authors 7–10). Relevant literature up to April 2017 was included with an emphasis on more recent publications; the document was revised again after the publication of the ASPRE trial in August 2017. The first version was circulated by email to all members in March 2017 and 8 subsequent versions emanated following email discussions to achieve consensus among the group. The document was then sent to all members of ISSHP Council for further comment and those who responded are listed in the acknowledgments below. The final version was concluded on December 28, 2017 and then amended after reviewers’ comments by March 1, 2018.

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S.A. Karumanchi received patents on biomarkers held by Harvard Medical School, Mohaupt, Switzerland; Prof Lucy Chappell, United Kingdom; Prof Mike Leichter. The other authors report no conflicts.


Hypertensive Disorders of Pregnancy: ISSHP Classification, Diagnosis, and Management

Recommendations for International Practice

Mark A. Brown, Laura A. Magee, Louise C. Kenny, S. Ananth Karumanchi, Fergus P. McCarthy, Shigeru Saito, David R. Hall, Charlotte E. Warren, Gloria Adoyi and Salisu Ishaku on behalf of the International Society for the Study of Hypertension in Pregnancy (ISSHP)

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