WHO RECOMMENDATIONS FOR PREVENTION AND TREATMENT OF PRE-ECLAMPSIA AND ECLAMPSIA

Implications and Actions

Background

Nearly one-tenth of maternal deaths in Asia and Africa and one-quarter of maternal deaths in Latin America are associated with hypertensive disorders of pregnancy. Among the hypertensive disorders, pre-eclampsia and eclampsia have the greatest impact on maternal and newborn morbidity and mortality. Yet the majority of deaths related to pre-eclampsia and eclampsia could be avoided if women received timely and effective care, delivered according to evidence-based standards.

Criteria for Diagnosis of Pre-eclampsia and Eclampsia

Pre-eclampsia:
Onset of a new episode of hypertension during pregnancy, characterized by:
• Persistent hypertension (diastolic blood pressure ≥ 90 mm Hg) and
• Substantial proteinuria (> 0.3 g/24 hours).

Eclampsia:
• Generalized seizures, generally in addition to pre-eclampsia criteria.

The primary goal of the WHO Recommendations for Prevention and Treatment of Pre-eclampsia and Eclampsia is to improve the quality of care and outcomes for pregnant women who develop the two most dangerous hypertensive disorders. While the recommendations are not intended to be comprehensive, they are intended to promote proven, evidence-based clinical practices in the management of women with pre-eclampsia and eclampsia.

Guideline Content and Development Process

WHO’s guidelines were developed in accordance with the WHO Handbook for Guideline Development, through a process involving: (1) identification of critical questions and critical outcomes; (2) retrieval of evidence; (3) assessment, grading, and synthesis of the evidence; (4) formulation of recommendations; and (5) planning for dissemination, implementation, impact evaluation, and updating. In addition to staff from the WHO Departments of Reproductive Health and Research, Making Pregnancy Safer, and Nutrition for Health and Development, many international stakeholders and external experts, including 173 participants in an online consultation and 25 experts at a technical consultation, were involved in the guideline development process. Evidence related to each specific question, drawn primarily from Cochrane reviews, was rigorously examined and graded according to its strength. Likewise, the strength of each recommendation was determined based on the grade of the evidence as well as the magnitude of the effect, the balance of advantages versus disadvantages, resource use, and feasibility.
## Clinical Practice Recommendations for the Prevention and Management of Pre-Eclampsia and Eclampsia (PE/E)

### During Antenatal Care

<table>
<thead>
<tr>
<th>Practices Recommended</th>
<th>Practices NOT Recommended</th>
<th>Practice Implication</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓ Calcium supplementation during pregnancy in areas where calcium intake is low (&lt;900 mg/day).</td>
<td>✗ Vitamin D supplementation during pregnancy.</td>
<td>Provide calcium to all women with low calcium intake and low-dose acetylsalicylic acid to selected groups for the prevention of PE/E. While vitamin supplementation can be useful for other health conditions, do not provide Vitamins C, D, or E, to pregnant women as part of a strategy for prevention of PE/E.</td>
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<tr>
<td>✓ Low-dose acetylsalicylic acid (aspirin, 75 mg) for the prevention of pre-eclampsia in women at high risk of developing the condition.</td>
<td>✗ Individual or combined vitamin C and vitamin E supplementation.</td>
<td>Give antihypertensive drugs, but not diuretics, to pregnant women with severe hypertension.</td>
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<tr>
<td>✓ Antihypertensive drugs for pregnant women with severe hypertension.</td>
<td>✗ Use of diuretics, particularly thiazides, for prevention of pre-eclampsia and its complications.</td>
<td>Do not advise rest or dietary salt restriction for pregnant women to prevent pre-eclampsia or its complications.</td>
</tr>
<tr>
<td>✓ In women with severe pre-eclampsia, if there is a viable fetus and the pregnancy is less than 37 weeks of gestation, expectant management can be considered, provided that uncontrolled maternal hypertension, increasing maternal organ dysfunction, and fetal distress do not occur and the conditions can be monitored.</td>
<td>✗ Advice to rest at home.</td>
<td>For a woman with severe pre-eclampsia during a preterm pregnancy (&lt; 37 weeks), clinicians can monitor the woman if: (1) her blood pressure is under control; (2) there is no fetal distress; and (3) there are no signs of maternal organ dysfunction. Continuous monitoring is necessary during this period of expectant management.</td>
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### During Labor and Birth

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<tr>
<td>✓ Induction of labor for women with severe pre-eclampsia at a gestational age when the fetus is not viable or is unlikely to achieve viability within one or two weeks.</td>
<td>Conduct an expedited delivery for women with severe pre-eclampsia remote from term, whether or not the fetus is viable.</td>
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<tr>
<td>✓ Expedited delivery for women with severe pre-eclampsia at term.</td>
<td>Magnesium sulfate is the anticonvulsant of choice for women with severe pre-eclampsia or eclampsia. If possible, give a full regimen of magnesium sulfate to women with eclampsia or severe pre-eclampsia. If the administration of a full regimen is not possible, these women should be given the loading dose of magnesium sulfate and should be immediately transferred to a higher-level health care facility for further treatment.</td>
</tr>
<tr>
<td>✓ Magnesium sulfate, in preference to other anticonvulsants, for the prevention of eclampsia in women with severe pre-eclampsia.</td>
<td>The full intravenous or intramuscular magnesium sulfate regimen for the prevention and treatment of eclampsia.</td>
</tr>
<tr>
<td>✓ Magnesium sulfate, in preference to other anticonvulsants, for treatment of women with eclampsia.</td>
<td>For women with severe pre-eclampsia or eclampsia, in settings where it is not possible to administer the full magnesium sulfate regimen, use the magnesium sulfate loading dose followed by immediate transfer to a higher-level health care facility.</td>
</tr>
<tr>
<td>✓ The full intravenous or intramuscular magnesium sulfate regimen for the prevention and treatment of eclampsia.</td>
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1. A full report of the recommendations can be found in WHO Recommendations for Prevention and Treatment of Pre-eclampsia and Eclampsia (http://whqlibdoc.who.int/publications/2011/9789241548335_eng.pdf), and a full listing of the evidence supporting these recommendations can be found in WHO Recommendations for Prevention and Treatment of Pre-eclampsia and Eclampsia: Evidence Base (http://whqlibdoc.who.int/hq/2011/WHO_RHR_11.25_eng.pdf).
CLINICAL PRACTICE RECOMMENDATIONS FOR THE PREVENTION AND MANAGEMENT OF PRE-ECLAMPSIA AND ECLAMPSIA (PE/E)

During Postpartum Care

<table>
<thead>
<tr>
<th>✓ Recommended Practices</th>
<th>Practice Implication</th>
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<tbody>
<tr>
<td>✓ Continued antihypertensive drugs during the postpartum period for women treated with antihypertensive drugs during the antenatal period.</td>
<td>Treat women with antihypertensive drugs during the postpartum period if they: (1) have severe postpartum hypertension; or (2) were treated with antihypertensive drugs during pregnancy.</td>
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<tr>
<td>✓ Antihypertensive drugs for women with severe postpartum hypertension.</td>
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Program Actions

The ultimate goal of these guidelines is to improve the quality of care and health outcomes related to pre-eclampsia and eclampsia. The recommendations, especially those that represent a change from previous practice, will require actions at the national, district, and local levels. The following actions are needed:

1. **Revise national guidelines or protocols to include evidence-based practices.**
   - Each country’s approach to promoting the use of the recommendations should be tailored to the specific national and local context. The revision of existing national guidelines should be a well-planned and participatory, consensus-driven process, and any modifications should be made in an explicit and transparent manner and based on clear justification. The revision process should include these steps:
     - Convene a national working group of recognized clinical experts from government agencies, medical and nursing/midwifery educational institutions, professional organizations, key nongovernmental organizations (NGOs), and other experts to review the WHO recommendations and consider what adaptations are necessary for the local context.
     - Develop clear and practical clinical protocols that reflect the recommendations.
     - Develop clear and practical guidance for community health workers.
     - Ensure that policies, including job descriptions, reflect the new recommendations.
       - Ensure that all skilled birth attendants are authorized to give magnesium sulfate and antihypertensives for severe pre-eclampsia and eclampsia.
       - Ensure that trained community health workers are authorized to counsel and provide calcium in areas of calcium deficiency.
     - Orient key governmental and NGO stakeholders and opinion leaders to the recommendations and their implications for practice in facilities and communities.
       - Ensure that stakeholders at the national, district, and community levels are included in the orientation.
       - Ensure that copies of the current guidelines are distributed to all facilities and educational institutions.

2. **Promote essential components that help ensure an enabling environment.**
   - Selected processes and procedures should be put in place to ensure an enabling environment for implementation of the recommendations.
   - Drugs such as magnesium sulfate, calcium gluconate, and antihypertensives (such as labetalol, hydralazine, nifedipine, or methyldopa), as well as appropriate formulations of calcium and acetylsalicylic acid, should be on the essential drug list.
   - Budgets and supply systems must accommodate continuous, ready access to essential drugs and supplies. Each site where antenatal or labor and delivery care is provided must have the following:
     - Functioning sphygmomanometers and stethoscopes;
     - Appropriate antihypertensive drugs, such as labetalol, hydralazine, nifedipine, or methyldopa;
     - Magnesium sulfate and calcium gluconate;
     - 10 mL and 20 mL syringes;
     - Normal saline or Ringer’s lactate IV solution;
     - Job aid for the administration of magnesium sulfate; and
     - An eclampsia box, which includes all needed drugs and equipment (syringe, swabs, intravenous line, etc.), as a practical solution to facilitate rapid action.
• Health care workers should be committed to evidence-based clinical practices.
  ▪ Antenatal care skills should include the provision of preventive supplements.
  ▪ All health care providers who care for pregnant women or women in labor must be
    competent to detect and manage pre-eclampsia and eclampsia, to prevent women with
    pre-eclampsia from developing eclampsia. Providers will also need the skills to induce
    labor, perform operative delivery, or refer women who need a higher level of care.
  ▪ Health care providers should avoid the use of treatments and drugs that have been shown
    to be ineffective or potentially harmful, and they should advocate against these practices
    in their facilities and among their colleagues.

• Evidence-based services should be established in the most peripheral settings that care for
  pregnant and laboring women, to ensure equitable access to services and help initiate emergency
  supportive care as early as possible when complications are detected.

3. Use participatory processes to change provider behavior with regard to evidence-based
   practices.
• Health care providers and other key stakeholders in government and NGOs should be involved in
  the process of guideline development and adaptation.
• Providers should be involved in establishing evidence-based standards of care and in the
  assessment of progress toward achieving the standards.
• The competencies necessary to achieve these standards should be taught in pre-service education
  and should be included in in-service training in facilities and communities as needed. Curricula
  may need to be developed or revised, teaching materials may need to be developed, and faculty
  and trainers may need to be trained.
• E-health and informatics reminders and decision support, audit-and-feedback, and supportive
  supervision should foster continuous improvement in the provision of quality care and should
  recognize quality when it is achieved.
• Professional networks and organizations can be enlisted to support implementation of evidence-
  based guidelines.
• Job aids should be available to remind providers of protocols and procedures.

4. Monitor and evaluate guideline implementation.
• Monitoring and evaluation systems must include appropriate indicators that are examined in a
  non-punitive manner and that can be used to guide the development, management, and scale-up
  of services. Ideally, implementation of the recommendations should be monitored at the health
  service level. Data can be supplemented with secondary analysis of administrative or clinical
  databases. Clearly defined indicators are needed and could be associated with locally determined
  targets. In this context, one critical indicator is suggested:
  ▪ The proportion of women with severe pre-eclampsia or eclampsia who receive magnesium
    sulfate therapy (calculated as the number of women with severe pre-eclampsia/eclampsia
    receiving magnesium sulfate over the total number of women who present with severe
    pre-eclampsia/eclampsia) (WHO Recommendations).
• Other “near miss” indicators should be considered, where feasible. For example:
  ▪ The proportion of pre-eclamptic women with severe hypertension who receive an anti-
    hypertensive agent over the total number of pre-eclamptic women with severe
    hypertension.
  ▪ These indicators provide an overall measure of the use of magnesium sulfate as the first option
    therapy for eclampsia, and appropriate use of antihypertensive agents. The use of other locally
    determined process indicators is also recommended, particularly for the assessment of the
    preventive use of magnesium sulfate and local protocol compliance during the loading and
    maintenance phases.