

Role of Low-Dose Aspirin in the Prevention of Pre-eclampsia: Current Guidelines, Evidence, and Implementation Challenges

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Abstract: Pre-eclampsia remains a major cause of maternal and perinatal morbidity and mortality globally, particularly in low- and middle-income countries. Low-dose aspirin (LDA) has emerged as a key preventive strategy due to its antiplatelet and anti-inflammatory properties. This review summarizes the pathophysiology of pre-eclampsia, the pharmacological rationale for aspirin uses, and the evidence supporting its efficacy. It also reviews current global and national guidelines on LDA use, optimal dosing strategies, and barriers to implementation in clinical settings, particularly in resource-limited environments. Effective implementation of LDA for pre-eclampsia prevention requires provider training, community awareness, and health system strengthening.

Keywords: Low-dose aspirin, Pre-eclampsia, Antenatal care, Hypertensive disorders of pregnancy, ACOG guidelines, ISSHP, Maternal morbidity

1. Introduction

Pre-eclampsia is a multisystem hypertensive disorder of pregnancy, characterized by new-onset hypertension and proteinuria or end-organ dysfunction after 20 weeks of gestation. It affects approximately 5–8% of pregnancies worldwide and contributes significantly to maternal and fetal mortality, particularly in low-resource settings. Emerging evidence has shown that early initiation of low-dose aspirin (LDA) in at-risk women can significantly reduce the incidence of pre-eclampsia. However, implementation in clinical practice faces multiple challenges despite clear recommendations from professional bodies such as ACOG, WHO, and FIGO.

2. Pathophysiology of Pre-eclampsia

Pre-eclampsia originates from abnormal placentation in early pregnancy, leading to impaired trophoblast invasion and inadequate remodeling of spiral arteries. This results in placental ischemia, which triggers the release of antiangiogenic factors, endothelial dysfunction, and systemic inflammation. These changes culminate in the clinical manifestations of hypertension, proteinuria, and multiorgan involvement.

3. Mechanism of Action of Low-Dose Aspirin

Aspirin irreversibly inhibits cyclooxygenase-1 (COX-1), thereby reducing the synthesis of thromboxane A₂, a potent vasoconstrictor and platelet aggregator. This shifts the prostacyclin-thromboxane balance in favor of vasodilation and reduced platelet aggregation. Low doses (75–150 mg) selectively inhibit thromboxane without significantly affecting prostacyclin, thus improving placental perfusion and reducing pre-eclampsia risk.

4. Evidence from Clinical Trials

The CLASP trial (1994) was among the first to assess aspirin in pre-eclampsia prevention and showed modest

benefit. More recently, the ASPRE trial (2017) demonstrated a 62% reduction in preterm pre-eclampsia with 150 mg aspirin initiated before 16 weeks in high-risk women. Meta-analyses, including Cochrane reviews, consistently support the early initiation (before 16 weeks) of LDA for optimal effect.

5. Current Global and National Guidelines

Several professional organizations recommend LDA for pre-eclampsia prevention in high-risk women:

- WHO recommends 75 mg aspirin daily from 12 weeks to delivery for women at high risk.
- ACOG advises 81 mg aspirin from 12–28 weeks (preferably before 16 weeks) in women with one high-risk or multiple moderate-risk factors.
- FIGO and NICE also endorse early aspirin use based on individual risk assessments.
- FOGSI (India) aligns with these global recommendations, supporting LDA use in high-risk pregnancies.

6. Clinical Use: Timing, Dose, and Indications

Aspirin should be started before 16 weeks of gestation (ideally between 12–14 weeks) for maximal efficacy. The dose ranges from 75 to 150 mg, with recent evidence favoring higher doses (e.g., 150 mg) for better outcomes. High-risk factors include a history of pre-eclampsia, multifetal gestation, chronic hypertension, diabetes, renal disease, and autoimmune disorders. Moderate-risk factors include nulliparity, obesity, advanced maternal age, and low socioeconomic status.

7. Barriers to Implementation

Despite strong evidence and guidelines, implementation of LDA in clinical practice faces multiple obstacles:

- Patient-level barriers: Late antenatal registration, poor health literacy, concerns about drug safety during pregnancy.
- Provider-level barriers: Inadequate knowledge of guidelines, inconsistent risk assessment, and lack of training.
- System-level barriers: Poor drug availability, fragmented health systems, lack of standardized protocols, and poor integration into ANC services.

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8.Strategies to Overcome Challenges

To enhance implementation, the following strategies are recommended:

- Training programs for healthcare workers on risk stratification and guideline adherence.
- Ensuring consistent availability of LDA at primary healthcare levels.
- Community-based awareness campaigns to encourage early ANC visits.
- Incorporating LDA prescription into national safe motherhood programs and ANC protocols.
- Use of mobile health (mHealth) tools for reminders and guideline dissemination.

9.Future Directions

Ongoing trials are exploring the role of aspirin in combination with other agents like calcium or statins. There is growing interest in pharmacogenomics to identify responders and in refining risk prediction models using biomarkers like PAPP-A, PlGF, and uterine artery Doppler indices. Further research is also needed on the efficacy of LDA in low-resource settings with high disease burden.

10. Conclusion

Low-dose aspirin is a proven, cost-effective intervention to prevent pre-eclampsia, especially in high-risk pregnancies. Timely initiation, appropriate dosing, and guideline-based risk assessment are key to its success. Addressing systemic and behavioral barriers through coordinated health system efforts can significantly improve maternal and perinatal outcomes.

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