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Review Article

A comprehensive review on hypertensive disorders of pregnancy: risk stratification, predictors and preventive strategies

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ABSTRACT

Hypertensive disorders of pregnancy (HDP), particularly pre-eclampsia, are important causes of maternal and perinatal morbidity and mortality. Because effective prevention must begin before clinical disease is established, antenatal care should include early risk assessment and timely initiation of evidence-based prophylaxis. Pre-eclampsia is a heterogeneous, multisystem disorder in which abnormal placentation and placental stress contribute to an imbalance between pro-angiogenic and anti-angiogenic factors, systemic endothelial dysfunction, and end-organ injury. This review summarises the pathophysiology of pre-eclampsia; examines clinical risk assessment, the HDP-Gestosis Score, mean arterial pressure (MAP), uterine artery Doppler and angiogenic biomarkers; and compares key recommendations from the World Health Organization (WHO) and the NICE/RCOG clinical framework. Low-dose aspirin is recommended for pregnant women at increased risk, with dose and timing determined by the applicable guideline and local protocol. Calcium supplementation is recommended by WHO in populations with low dietary calcium intake. Combined clinical and first-trimester multimarker screening can improve identification of pregnancies at risk of preterm pre-eclampsia, but no screening test replaces ongoing blood-pressure assessment and clinical surveillance. Implementation should prioritise validated tools, clear referral pathways, equitable access to antenatal care and accurate counselling.

Keywords: Pre-eclampsia, Hypertensive disorders of pregnancy, Risk stratification, Gestosis score, Aspirin, Calcium, Placental growth factor, Mean arterial pressure

INTRODUCTION

Hypertensive disorders of pregnancy comprise chronic hypertension, gestational hypertension, pre-eclampsia (including pre-eclampsia superimposed on chronic hypertension) and eclampsia. They remain major contributors to maternal and perinatal complications worldwide, with a particularly high burden where antenatal detection, emergency obstetric care and referral systems are limited.[1–4] Definitions and classification should follow a recognised guideline. Pre-eclampsia generally presents after 20 weeks with new-onset hypertension accompanied by proteinuria and/or maternal organ dysfunction; proteinuria is not obligatory when other diagnostic features are present.[3,4] Early identification matters because aspirin prophylaxis is most effective when started early in pregnancy, while structured surveillance enables timely recognition of maternal deterioration and fetal growth restriction.

PATHOPHYSIOLOGY AND ANGIOGENIC IMBALANCE

Pre-eclampsia is commonly described using a two-stage model, although its biology is heterogeneous. In normal placentation, extravillous trophoblasts remodel the maternal spiral arteries into low-resistance vessels that

support uteroplacental perfusion. In a proportion of affected pregnancies, placentation and vascular remodelling are incomplete. Placental malperfusion, oxidative stress and cellular stress can then promote the release of anti-angiogenic and inflammatory mediators into the maternal circulation.[5–8]

Soluble fms-like tyrosine kinase-1 (sFlt-1) binds vascular endothelial growth factor (VEGF) and placental growth factor (PlGF), reducing their bioavailability. Soluble endoglin may also contribute to endothelial dysfunction. The resulting disturbance in angiogenic signalling is associated with vasoconstriction, increased vascular permeability, platelet and coagulation abnormalities, and renal, hepatic, neurological or haematological involvement.[6–8] These pathways explain why pre-eclampsia is a multisystem syndrome rather than simply hypertension with proteinuria. Maternal cardiovascular, metabolic, immune and genetic factors modify the clinical phenotype.

CLINICAL RISK STRATIFICATION

Risk assessment should begin at booking and be revisited when new information emerges. Clinical history is inexpensive and widely available, but it has limited sensitivity when used alone. Risk factors are generally classified as high-risk or moderate-risk to guide aspirin prophylaxis. Under NICE guidance, one high-risk factor or more than one moderate-risk factor supports offering aspirin.[9]

High-risk factors

Commonly recognised high-risk factors include pre-eclampsia or hypertensive disease in a previous pregnancy, chronic hypertension, chronic kidney disease, pre-existing type 1 or type 2 diabetes, and autoimmune disease such as systemic lupus erythematosus or antiphospholipid syndrome.[9,10] Local guidelines may include additional factors or use a different risk-assessment algorithm.

Moderate-risk factors

Moderate-risk factors in NICE guidance include nulliparity, maternal age 40 years or older, an inter-pregnancy interval longer than 10 years, body mass index (BMI) of at least 35 kg/m² at the first visit, a family history of pre-eclampsia, and multifetal pregnancy.[9] Other factors, including assisted conception, adverse obstetric history and social or demographic determinants, may be incorporated in particular models, but their classification varies by guideline. A risk factor should not be described as an independent predictor unless supported by appropriate evidence.

HDP-Gestosis Score

The HDP-Gestosis Score is a clinical risk-scoring approach developed and used in Indian antenatal settings. It assigns weighted points to selected maternal characteristics and clinical conditions, with a cumulative score used to identify women who may benefit from intensified surveillance and prophylaxis. A prospective study published in the Journal of Obstetrics and Gynaecology of India reported useful predictive performance for a score threshold of 3 or more; however, performance estimates are dependent on the study population, prevalence, definitions and implementation.[11]

Published descriptions of the score should be followed exactly when it is applied clinically. Lists of factors and point allocations reproduced in secondary sources are not always consistent. Therefore, this review does not reproduce an unverified exhaustive item-by-item scoring table. Before publication, the authors should insert the scoring table from the original FOGSI-approved source or the specific validation study used by their institution. The score should be regarded as a risk-assessment aid, not a diagnostic test, and should not replace established guideline criteria or clinical judgement.

BIOPHYSICAL AND BIOCHEMICAL PREDICTORS

Mean arterial pressure

Mean arterial pressure reflects systemic vascular resistance and can contribute to first-trimester screening. Accurate measurement requires an appropriately sized cuff, a validated device, a standardised resting position and repeated readings according to the screening protocol. MAP is more informative when combined with maternal characteristics and other markers than when interpreted as a stand-alone test.[12,13]

Uterine artery Doppler

Uterine artery pulsatility index (UtA-PI), measured during the first-trimester screening window in an appropriately trained service, provides an indirect assessment of uteroplacental vascular resistance. Increased resistance is associated particularly with preterm or early-onset pre-eclampsia. Performance depends on gestational age, technique, operator training and the screening algorithm. Bilateral notching alone should not be treated as a definitive diagnosis.

Placental and angiogenic biomarkers

PlGF is a pro-angiogenic placental protein, and lower concentrations are associated with an increased risk of pre-eclampsia. sFlt-1 is anti-angiogenic; an increased sFlt-1/PlGF ratio may support assessment of suspected pre-eclampsia in selected clinical settings. Biomarker assays and thresholds are platform- and gestation-specific. A high negative predictive value reported for a particular ratio and short-term clinical question must not be generalised to all populations, gestational ages or longer follow-up periods.[7,8,14]

First-trimester combined screening integrates maternal factors with MAP, UtA-PI and placental biomarkers such as PlGF. In the ASPRE trial, women identified as being at high risk of preterm pre-eclampsia by a combined algorithm were randomised to aspirin 150 mg daily or placebo; aspirin reduced the incidence of preterm pre-eclampsia.[12,13] This supports combined screening where resources and expertise are available, while clinical risk-factor assessment remains important in settings where biomarker testing is unavailable.

Emerging predictors and precision approaches

Research into lipid profiles, glucose and insulin regulation, inflammatory pathways, renal tubular injury markers, circulating RNA, proteomics and metabolomics may improve understanding of disease heterogeneity. Machine-learning models may identify interactions that are difficult to capture with conventional scoring systems. Nevertheless, many emerging markers remain investigational: external validation, calibration, reproducibility, clinically meaningful thresholds, cost-effectiveness and impact on outcomes are required before routine adoption. Claims that a novel marker is a reliable screening test should be supported by prospective validation rather than discovery-stage associations alone.

PREVENTIVE STRATEGIES

Low-dose aspirin

Aspirin irreversibly inhibits platelet cyclo-oxygenase-1 and reduces thromboxane A_2 synthesis. At low doses, it alters the balance of platelet and vascular prostanoids and can reduce the risk of preterm pre-eclampsia in appropriately selected high-risk pregnancies. Prescribing should follow the relevant national or institutional guideline, considering contraindications, bleeding risk, allergy and the patient's clinical circumstances.

WHO recommends low-dose aspirin for women at high risk, initiated by 20 weeks of gestation or as soon as antenatal care begins when appropriate.[15] NICE recommends 75–150 mg daily from 12 weeks until birth for women with one high-risk factor or more than one moderate-risk factor.[9] The ASPRE trial used 150 mg nightly from 11–14 weeks until 36 weeks in women identified by a combined first-trimester screening algorithm.[12] These recommendations are not identical; therefore, a manuscript should not attribute a universal 150-mg regimen or a stop-at-36-weeks rule to all organisations. The selected dose and stopping point should be explicitly linked to the guideline followed locally.

Calcium supplementation

WHO recommends calcium supplementation during pregnancy in populations with low dietary calcium intake to reduce the risk of pre-eclampsia. The commonly cited regimen is 1.5–2.0 g of elemental calcium per day, divided into doses, according to local protocols and the applicable WHO recommendation.[16] Calcium supplementation should be considered in the context of baseline dietary intake, total intake from supplements and food, tolerability and individual clinical factors. It should not be presented as a universal substitute for aspirin in women at increased risk.

Antenatal surveillance and service delivery

Prevention also requires reliable blood-pressure measurement at antenatal contacts, assessment for symptoms and end-organ involvement when indicated, evaluation of fetal growth and wellbeing, and clear pathways for escalation and referral. Women should be counselled to seek urgent assessment for severe headache, visual disturbance, severe epigastric or right-upper-quadrant pain, breathlessness or other concerning symptoms. Routine bed rest, salt restriction solely to prevent pre-eclampsia, or unproven supplements should not be promoted as preventive interventions.[9]

Table 1: Comparison of selected guideline approaches.

Guideline / approach	Risk identification	Prevention points
WHO	Clinical identification of women at high risk; adapt delivery to local context.	Low-dose aspirin for women at high risk; calcium supplementation in populations with low dietary calcium intake.
NICE (UK; commonly used alongside RCOG practice)	One high-risk factor or more than one moderate-risk factor.	Aspirin 75–150 mg daily from 12 weeks until birth.
FIGO first-trimester approach	Combined screening using maternal factors, MAP, UtA-PI and PlGF where available.	For screen-positive women, aspirin 150 mg nightly from 11–14 weeks to 36 weeks is supported by the ASPRE trial-based pathway.
HDP-Gestosis Score	Point-based clinical assessment; evidence includes Indian validation studies.	Use as a supplementary risk tool according to the validated local scoring source; do not substitute for national guidance.

CONCLUSION

Pre-eclampsia is a heterogeneous placental and maternal vascular disorder that requires early risk identification, prevention and ongoing surveillance. Maternal clinical history remains the foundation of risk assessment; MAP, uterine artery Doppler and placental biomarkers can improve prediction when integrated into validated screening algorithms. The HDP-Gestosis Score may offer a pragmatic option in Indian settings, but its components and threshold should be taken from an authoritative source and interpreted in light of the available validation evidence. Low-dose aspirin for eligible women and calcium supplementation in populations with low dietary calcium intake are key evidence-based preventive measures. Consistent implementation, clear counselling and timely referral are essential to translating risk prediction into improved maternal and perinatal outcomes.

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