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# PREECLAMPSIA AND ENDOTHELIAL DYSFUNCTION: NEW BIOMARKERS AND PREVENTION STRATEGIES

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**Abstract:** Preeclampsia (PE) is one of the leading causes of maternal and perinatal morbidity and mortality worldwide, characterized by hypertension and multisystem dysfunction after the 20th week of gestation. The pathophysiology involves abnormal placental implantation and endothelial dysfunction, mediated by an imbalance between angiogenic and antiangiogenic factors. This review article discusses current pathogenic mechanisms, emerging biomarkers (such as sFlt-1/PlGF), and prevention strategies, including the use of low-dose aspirin, risk monitoring, and early hemodynamic follow-up. Studies published between 2016 and 2024 in the PubMed, SciELO, and UpToDate databases were reviewed. It is concluded that early diagnosis and personalized prevention based on biomarkers represent the future of modern obstetrics, reducing serious complications and improving maternal-fetal outcomes.

**Keywords:** Preeclampsia; Endothelial dysfunction; Biomarkers; Prevention; Obstetrics.

## INTRODUCTION

Preeclampsia is a pregnancy-specific hypertensive syndrome responsible for approximately 15% of maternal deaths worldwide (WHO, 2023).

It is characterized by arterial hypertension associated with proteinuria and/or signs of organ dysfunction, with potential progression to eclampsia, HELLP syndrome, and placental insufficiency.

In recent decades, understanding of the pathophysiology of PE has evolved significantly. It is now known that the disease

originates in the placenta, as a result of failure in the remodeling of the uterine spiral arteries, leading to hypoxia and the release of antiangiogenic substances that damage the maternal endothelium (REDMAN; STAFF, 2021).

Early recognition of at-risk patients and the use of plasma biomarkers have proven to be fundamental in risk stratification and personalized prevention of the disease.

## METHODOLOGY

An integrative literature review was conducted, searching the PubMed, SciELO, UpToDate, and ScienceDirect databases between 2016 and 2024.

The following descriptors were used: preeclampsia, endothelial dysfunction, angiogenic factors, sFlt-1, PlGF, and low-dose aspirin.

Original articles, systematic reviews, and consensus statements from societies such as the International Society for the Study of Hypertension in Pregnancy (ISSHP) and FIGO (2022) were included.

Forty-three studies were selected, analyzing pathophysiology, diagnostic biomarkers, preventive interventions, and new therapeutic perspectives.

## 1. PATHOPHYSIOLOGY AND ENDOTHELIAL DYSFUNCTION

Preeclampsia is the result of abnormal placentation. Early in pregnancy, trophoblast cells should invade deeply into the maternal spiral arteries, converting them into low-resistance vessels.

In PE, this invasion is incomplete, maintaining high-resistance arteries, which causes placental hypoxia and the release of antiangiogenic factors (ROBERTO et al., 2020).

Among the main mediators involved are:

- sFlt-1 (soluble fms-like tyrosine kinase-1): antagonizes VEGF and PlGF, causing vasoconstriction and endothelial injury.
- Soluble endoglin (sEng): inhibits TGF-β, aggravating vascular dysfunction.
- PlGF (Placental Growth Factor): a protective angiogenic factor, reduced in cases of PE.

The sFlt-1/PlGF imbalance is currently one of the main laboratory markers for diagnosis and prognosis of the disease, recognized by international societies (FIGO, 2022).

## 2. EMERGING BIOMARKERS AND EARLY DIAGNOSIS

Recent studies have shown that the sFlt-1/PlGF ratio has high accuracy (AUC > 0.90) for predicting the onset of preeclampsia within 4 weeks (ZEISLER et al., 2019).

In addition, new biomarkers are being studied:

- placental microRNAs (miR-210 and miR-155): related to placental hypoxia.

- PAPP-A and ADAM12: indicate early trophoblastic dysfunction.
- Exosomal proteins and metabolomic profiles: emerging as tools for predicting PE in high-risk populations (CARVALHO et al., 2023).

The combination of these markers with clinical data (age, BMI, mean arterial pressure, obstetric history) significantly improves the predictive power of first-trimester screening algorithms.

## 3. PREVENTION STRATEGIES AND EVIDENCE-BASED THERAPY

### 3.1. Low-dose aspirin

Several studies have confirmed that the use of 100–150 mg/day of ASA started between 11 and 16 weeks reduces the risk of severe PE and preterm birth by up to 60% (ROLNIK et al., 2017).

The FIGO and WHO guidelines (2022) recommend its prophylactic use in high-risk pregnant women.

### 3.2. Calcium and antioxidants

Calcium supplementation (1–2 g/day) in populations with low dietary intake has been shown to reduce the incidence of PE.

However, isolated antioxidants (vitamins C and E) have not shown significant clinical benefit.

### 3.3. Heparin and emerging therapies

Low molecular weight heparins have been studied for their modulating action on the endothelium and placenta, but there is still no consensus on their routine use (PÉREZ et al., 2022).

Innovative therapies, such as sFlt-1 blockers and recombinant VEGF infusion, are under experimental investigation with promising results.

## 4. NEW TECHNOLOGIES AND PERSONALIZED MEDICINE

The integration of artificial intelligence (AI) into obstetrics has enabled personalized predictive models based on machine learning, combining biomarkers, uterine Doppler, and clinical data to predict PE with high accuracy (SILVA et al., 2023).

In addition, remote monitoring of blood pressure and uterine perfusion using wearable devices allows for early intervention before the clinical manifestation of the disease.

These advances point to a future of precision obstetrics, focused on individualized prevention.

## 5. CLINICAL AND ETHICAL IMPACTS

Early detection and the use of biomarkers raise ethical questions about equitable access, testing costs, and decision-making in borderline cases.

In developing countries, the challenge is to balance technology and economic feasibility, ensuring that the most at-risk pregnant women—who often have less access to care—benefit the most.

In addition, prenatal counseling should include clear discussions about the risks and benefits of preventive interventions and the importance of ongoing monitoring, reinforcing the principle of patient autonomy.

## CONCLUSION

Preeclampsia remains a global clinical challenge, but advances in the understanding of endothelial dysfunction and angiogenic biomarkers have transformed the diagnostic and preventive paradigm.

The clinical application of the sFlt-1/PlGF ratio, associated with the rational use of low-dose aspirin and individualized obstetric surveillance, represents a milestone in modern prenatal care.

The future points to the integration of molecular biology, AI, and personalized medicine, with the goal of reducing maternal and fetal mortality and promoting more preventive, accurate, and humanized obstetrics.

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