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Beyond Blood Pressure and Proteinuria: Integrating Endothelial Dysfunction and Hypercoagulability Biomarkers for Early Preeclampsia Prediction and Precision-Guided Maternal–Fetal Care

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Abstract

Preeclampsia continues to be a major cause of maternal and perinatal illness and death, especially in areas with restricted access to sophisticated prenatal diagnostics and urgent obstetric services. Traditional evaluation relying on blood pressure, protein levels in urine, and dysfunction of maternal organs might detect the condition only after pathological changes have occurred, emphasizing the necessity for enhanced early prediction and risk classification. This narrative review explores the possible combination of biomarkers for endothelial dysfunction and hypercoagul ability to enhance preeclampsia prediction and facilitate precision-guided maternal–fetal care. Angiogenic biomarkers, especially placental growth factor (PlGF), soluble fms-like tyrosine kinase-1 (sFlt-1), and the sFlt-1/PlGF ratio, offer clinically significant insights into placental dysfunction and immediate disease risk. Other endothelial markers, such as soluble endoglin and von Willebrand factor, might indicate vascular damage, but their added clinical significance is still not clearly defined. Haemostatic markers such as platelet count, D-dimer, fibrinogen, and thrombin-generation indicators can enhance clinical evaluation, but their utility is restricted by physiological changes during pregnancy, assay inconsistency, and variable predictive accuracy. A cohesive framework that incorporates maternal risk factors, clinical observations, angiogenic dysregulation, chosen hemostatic indicators, and fetale valuations might enhance personalized monitoring and referral choices.

Keywords: Preeclampsia; endothelial dysfunction; hypercoagulability; angiogenic biomarkers; precision obstetric care.

Introduction

Preeclampsia is a complex hypertensive condition during pregnancy and a significant factorin maternal and perinatal illness and death globally. Clinical symptoms can vary from newly developed hypertension and proteinuria to serious neurological issues, liver and kidney dysfunction, low platelet count, placental insufficiency, restricted fetal growth, and early delivery. The repercussions are especially severe in low- and middle-income nations, where restricted diagnostic capabilities, postponed referrals, and insufficient access to emergency obstetric services can raise the likelihood of preventable maternal and fetal fatalities [1-3]. Traditional evaluation depends on measuring blood pressure, assessing protein levels in urine, observing maternal symptoms, and identifying signs of organ dysfunction. While these indicators are essential for diagnosis and management, they might not sufficiently reflect the biological processes occurring before clinical deterioration. Proteinuria is not necessary for diagnosing preeclampsia if other qualifying signs of maternal organ dysfunction exist, whereas hypertension alone does not consistently differentiate pregnancies that may advance to severe illness. Thus, a significant unmet demand is the creation of dependable, biologically based methods that recognize high-risk pregnancies prior to the onset of irreversible maternal or placental issues [4-6].

Placental dysfunction, imbalance in angiogenesis, inflammation throughout the body, and injury to the endothelium are key factors in the pathophysiology of preeclampsia. Diminished trophoblast invasion and insufficient remodeling of spiral arteries can jeopardizeutero placental perfusion, leading to placental stress and the secretion of circulating antiangiogenic factors. Soluble fms-like tyrosine kinase-1 (sFlt-1) inhibits vascular endothelial growth factor and placental growth factor (PlGF), impairing endothelial balance and leading to vasoconstriction, heightened vascular permeability, and maternal organ damage. Lowered PlGF levels and a heightened sFlt-1/PlGF ratio may occur before clinical symptoms, offering a biological foundation for earlier risk evaluation. Clinical research has confirmed the significance of angiogenic biomarkers, especially the sFlt-1/PlGF ratio, as additional tools in assessing women with potential preterm preeclampsia [7-8].

Simultaneously, endothelial damage influences platelet activation, thrombin production, fibrin generation, and modified fibrinolysis to create hemostatic irregularities. Despite the natural hypercoagulablestate during pregnancy, preeclampsia can exacerbate coagulation activation and microvascular impairment, leading to placental insufficiency and maternal issues. Count of platelets, fibrinogen levels, D-dimer, and certain indicators of coagulation activation can thus yield additional insights [9-10]. Nonetheless, their understanding is made complex by gestational alterations, concurrent anomalies in different obstetric conditions, and variable proof of distinct predictive significance. In advanced disease, activation of hemostasis can lead to consumptive coagulopathy, highlighting the necessity to differentiate between early risk prediction and the evaluation of existing complications [11]. This narrative review critically analyzes the biological basis, clinical data, and translational possibilities of incorporating biomarkers for endothelial dysfunction and hypercoagulability in predicting early preeclampsia.

Methods

A narrative literature review method was employed to integrate findings related to endothelial dysfunction, angiogenic imbalance, hypercoagulability, and biomarker-based prediction of preeclampsia. The pertinent literature was conceptually structured into five categories: disease pathophysiology, biomarker efficacy, prediction of disease onset, evaluation of existing disease, and application in clinical practice. Emphasis was placed on peer-reviewed clinical studies, systematic reviews, international guidelines, and research assessing angiogenic biomarkers, coagulation irregularities, maternal results, and fetal results. The synthesis

analyzed research that included pregnant women at various gestational stages, such as asymptomatic individuals undergoing risk evaluations, those with suspected preeclampsia, and patients with a confirmed diagnosis. Special focus was placed on the sFlt-1/PlGF ratio, PlGF-based assessments, soluble endoglin, endothelial activation, platelet indices, fibrin-related indicators, and coagulation irregularities. The evidence was analyzed based on clinical objectives, study demographics, gestational age, assay features, and reported results. Diagnostic precision, prognostic distinction, calibration, and established clinical usefulness were regarded as separate performance metrics. Due to the nature of this being a narrative review instead of a systematic review with reproducible criteria for study selection and quantitative analysis, no formal pooled estimates or fabricated study-selection numbers are included.

Pathophysiological foundations of integrated biomarker prediction

1 Placental dysfunction and angiogenic imbalance

Preeclampsia typically arises from abnormal placental attachment, disrupted remodeling of spiral arteries, and insufficient uteroplacental blood flow. These processes may lead to placental stress, oxidative damage, and the discharge of soluble factors into the maternal bloodstream. The resultant maternal syndrome showcases the interplay of placental signals, maternal vascular vulnerability, immune reactions, and systemic endothelial impairment [12]. The antiangiogenic protein sFlt-1 attaches to circulating VEGF and PlGF, decreasing their accessibility for endothelial signaling. PlGF aids in angiogenesis and vascular changes during pregnancy; lower levels may suggest placental issues and disrupted angiogenic equilibrium. Increased sFlt-1 levels and decreased PlGF can occur prior to clinical symptoms, establishing a biological opportunity for risk evaluation before severe hypertension or organ damage is evident [13]. Nonetheless, an imbalance in angiogenesis does not equate to unavoidable clinical disease. Its understanding is influenced by gestational age, the degree and timing of placental dysfunction, maternal traits, and the clinical inquiry posed. Biomarkers should be combined with recognized risk factors and clinical observations instead of being viewed as standalone predictors of outcome.

2 Endothelial injury and systemic vascular dysfunction

The maternal endothelium controls vascular tone, permeability, inflammation, platelet adhesion, and coagulation. In preeclampsia, altered nitric oxide signaling, heightened oxidative stress, inflammatory response, and disrupted angiogenesis lead to vasoconstriction, capillary leakage, and vascular instability [14]. These alterations assist in clarifying the clinical variety of preeclampsia. Damage to renal endothelial cells may lead to proteinuria and reduced filtration, while dysfunction of cerebral vessels can cause severe headaches, visual problems, seizures, or strokes. Increased liver enzymes and thrombocytopenia can be associated with damage to hepatic endothelium and microvasculature. Vascular dysfunction of the placenta may hinder fetal growth and elevate the chances of medically necessary preterm delivery [15]. One marker cannot consistently capture these specific manifestations of the organs. Integrating angiogenicmetrics with clinical findings and pertinent organ-function assessments could thus enhance risk evaluation. However, the worth of a combined panel relies on its ability to enhance predictions beyond the data already obtained from standard evaluations.

3 Hypercoagulability and haemostatic dysregulation

Atypical pregnancy is linked to heightened levels of various coagulation factors, decreased function of certain natural anticoagulant mechanisms, and lowered fibrinolytic capacity. These bodily changes aid in reducing bleeding during delivery yet also make it more difficult to analyze coagulation biomarkers [16-17]. Preeclampsia can exacerbate haemostatic activation dueto endothelial damage, platelet activation, inflammation, and placental vascular disorders. Platelets engage with injured endothelium,

whereas tissue factor-driven thrombin production facilitates fibrin development. Dysfunction of the microvasculature might playa role in placental insufficiency and injury to maternal organs. Hypercoagulability must not be seen as a consistent or permanent condition [18]. Severe preeclampsia, placental abruption, significant hemorrhage, and disseminated intravascular coagulation can lead to the consumption of platelets and coagulation factors. A woman may therefore advance from heightened thrombotic tendency to important clinical coagulopathy. Biomarker analysis should differentiate between normal pregnancy changes, disease-related activation, and severe depletion [19]. The combination of endothelial and haemostatic biomarkers is biologically appealing due to the interconnection of these pathways. Determining whether this integration yields clinically significant predictive benefits necessitates direct empirical evaluation [20].

Endothelial and angiogenic biomarkers for early prediction (Table 1)

1 Placental growth factor

PlGF is among the most significant biomarkers for assessing placental dysfunction. Decreased levels of circulating PlGF are linked to compromised placental angiogenesis and a higher likelihood of preeclampsia, fetal growth restriction, and additional placental issues [21]. PlGF-based testing is especially useful when there is a suspicion of preterm preeclampsia. Depending on the test and gestational age, a low level can aid in evaluating women who might need increased monitoring or further examination. Its clinical value is partly in aiding the identification of women at relatively low short-term risk when results are positive and the broader clinical evaluation aligns with outpatient care [22]. A low PlGF concentration alone does not confirm the diagnosis, and a reassuring finding cannot counteract severe hypertension, neurological symptoms, abnormal organ function tests, or fetal distress. Performance is influenced by gestational age, specific assay thresholds, pre-existing kidney conditions, and the demographic being evaluated [23]. In early-pregnancy screening, PlGF provides more valuable information when integrated into a validated risk model that takes into account maternal traits and, when accessible, uterine artery Doppler results and mean arterial pressure. This contrasts with its application in symptomatic women during later stages of pregnancy, where the goal might be to evaluate the probability of developing preeclampsia within a specific short-term timeframe [24].

2 Soluble fms-like tyrosine kinase-1

sFlt-1 is a factor that inhibits angiogenesis and is involved in the maternal endothelial syndrome. Increased circulating levels indicate heightened anti-angiogenic activity and may be associated with deteriorating placental function [25]. Its main drawback as a standalone biomarker is that levels can fluctuate depending on gestational age and clinical severity. A significant value might suggest considerable placental stress, but its predictive significance relies on when the measurement is taken and the existence of other clinical irregularities. Thus, measuring sFlt-1 in isolation might provide less insight than evaluating its correlation with PlGF [26].

3 The sFlt-1/PlGF ratio

The sFlt-1/PlGF ratio is one of the most well-established biomarker methods for assessing suspected preeclampsia. It merges an antiangiogenic signal with a proangiogenic marker, offering an assessment of angiogenic imbalance. The PROGNOSIS study by Zeisler and associates showed that in women with suspected preeclampsia between 24 weeks and 36 weeks plus 6 days of gestation, an sFlt-1/PlGF ratio of 38 or less had a strong negative predictive value for excluding preeclampsia within one week. In that study population, the negative predictive value reported was 99.3%. A ratio exceeding 38 showed a significantly reduced positive predictive value for forecasting preeclampsia within four weeks, recorded at 36.7% [27]. These findings highlight an important difference: the ratio could be especially helpful for short-term disease exclusion in well-chosen populations, but an elevated ratio does not

confirm that preeclampsia will necessarily occur. Predictive values are influenced by disease prevalence, eligibility requirements, gestational age, and the context of testing. Cutoff values are also dependent on the assay and indication; the threshold of 38 should not be regarded as universal for every platform or clinical application [28]. The ratio can aid in decisions regarding surveillance, referral, and additional evaluation, but it should not solely dictate the timing of delivery. The mother's health, the baby's condition, the weeks of pregnancy, and the existing treatment protocols are all crucial.

4 Soluble endoglin

Soluble endoglin serves as an antiangiogenic and endothelial-associated biomarker linked to placental impairment and severe preeclampsia. Experimental and clinical findings indicate that it could disrupt transforming growth factor-β-related vascular signaling and lead to compromised endothelial function [29]. Its possible significance is in offering insights regarding vascular damage that could enhance sFlt-1 and PlGF. Nonetheless, its regular clinical function is still not well-defined, and issues like standardization, assay accessibility, and additional predictive effectiveness need more exploration. Soluble endoglin should thus be viewed as a promising research indicatori nstead of a confirmed substitute for validated angiogenic assessments [30].

5 Von Willebrand factor and endothelial activation

Von Willebrand factor (vWF) plays a role in platelet adhesion and clotting and may indicate endothelial activation. Elevated levels have been noted in preeclampsia, aligning with vascular damage and hemostatic disruption [31]. Nonetheless, vWF is affected by inflammation, normal pregnancy, blood type, and various other medical situations. While it might offer mechanistic understanding, its capacity to enhance early prediction beyond clinical risk factors and angiogenic biomarkers isstill uncertain. Additional indicators linked to the endothelium, such as soluble adhesion molecules and indicators of glycocalyx damage, also need prospective assessment prior to regular application [32-33].

Table 1. Endothelial and Angiogenic Biomarkers for Early Preeclampsia Prediction

Biomarker	Biological significance	Predictive potential	Key limitation
Placental growth factor (PlGF)	Proangiogenic placental protein	Low levels indicate placental dysfunction and support short-term risk assessment	Gestational age and assay-dependent thresholds
Soluble fms-like tyrosine kinase-1 (sFlt-1)	Antiangiogenic factor that inhibits VEGF and PlGF signalling	Elevated levels indicate angiogenic imbalance	Limited specificity when used alone
sFlt-1/PlGF ratio	Integrates antiangiogenic and proangiogenic activity	Supports short-term assessment of suspected preterm preeclampsia	Cutoffs depend on assay, gestational age, and clinical indication
Soluble endoglin	Interferes with endothelial and transforming growth factor-β-related signalling	Potential marker of vascular injury and disease severity	Limited routine validation and availability
Von Willebrand factor (vWF)	Mediates platelet adhesion and reflects endothelial activation	May indicate endothelial injury and haemostatic activation	Influenced by inflammation, pregnancy, and other conditions

Soluble adhesion molecules (e.g., sVCAM-1, sICAM-1)	Reflect endothelial activation and leukocyte–endothelial interactions	Potential indicators of vascular inflammation	Insufficient evidence for independent clinical prediction
Endothelial glycocalyx injury markers	Reflect disruption of the endothelial surface barrier	Potential indicators of vascular permeability and systemic endothelial damage	Mainly investigational; limited standardized assays

Abbreviations: ICAM-1, intercellular adhesion molecule-1; PlGF, placental growth factor; sFlt-1, soluble fms-like tyrosine kinase-1; sICAM-1, soluble ICAM-1; sVCAM-1, soluble vascular cell adhesion molecule-1; VEGF, vascular endothelial growth factor; vWF, von Willebrand factor

Hypercoagulability biomarkers and their prognostic potential (Table 2)

1 Platelet count and platelet indices

Thrombocytopenia is a recognized sign of serious illness when related to preeclampsia and is part of the evaluation of maternal organ impairment. Platelet counts can decrease due to activation, consumption, and interactions within the microvasculature. Repeated measurements can aid in recognizing decline, especially when analyzed in conjunction with blood pressure, liver enzymes, kidney function, and clinical signs [34]. Mean platelet volume and platelet distribution width have been explored as markers of platelet activation and turnover. Nevertheless, their results vary among studies, and values are influenced by lab analyzers, sample processing, gestational age, and underlying health issues. These indices lack adequate standardization to function as standalone screening tests [35]. The suitable clinical strategy is to focus on platelet count and its trend, employing other platelet indices only after confirming their local analytical validity and additional value.

2 D-dimer and fibrinogen

D-dimer indicates the degradation of cross-linked fibrin and may suggest elevated levels of fibrin formation and breakdown. Concentrations typically rise during pregnancy, especially as gestation progresses, reducing the applicability of non-pregnancy reference intervals [36]. Even though high D-dimer levels are linked to preeclampsia and the severity of the disease, their specificity is not sufficient for independent forecasting. Infection, thrombosis, hemorrhage, and various inflammatory or obstetric conditions can also increase concentrations. As a result, D-dimer ought not to be utilized as a sole biomarker for preeclampsia screening or analyzed with an unverified universal pregnancy threshold [37]. Fibrinogen levels typically increase during pregnancy. A decreasing concentration in a woman experiencing severe preeclampsia, placental abruption, or suspected disseminated intravascular coagulation could be more alarming than a single increase. Interpretation must thus take into account the clinical setting, sequential testing, platelet levels, prothrombin time, activated partial thromboplastin time, and signs of hemorrhage or organ failure [38].

3 Thrombin generation and platelet activation

Thrombin-generation tests, thrombin–antithrombin complexes, prothrombin fragment 1+2, and certain platelet-activation indicators provide more precise insights into the activation of coagulation pathways. These actions might assist in depicting the connection between endothelial damage and coagulation issues [39]. Nonetheless, their application in predicting preeclampsia is still predominantly experimental. The availability of assays, pre-analytical sensitivity, absence of standardized pregnancy-specific thresholds, and uncertainty about the implications of clinical decisions restrict regular implementation. Their most direct impact lies in mechanistic research and the creation of more reliably validated multivariable prediction models [40].

4 Distinguishing risk prediction from coagulopathy diagnosis

A critical clinical differentiation is that the biomarkers for predicting preeclampsia do not have to be identical to those utilized for assessing existing coagulopathy. Angiogenic indicators could aid in evaluating placental disorders, whereas coagulation assessments are generally most beneficial in cases of suspected bleeding, thrombosis, placental abruption, significant thrombocytopenia, liver dysfunction, or disseminated intravascular coagulation [41]. Thus, a combined biomarker panel should be developed with a particular clinical question in mind instead of being broadened without consideration. Increased measurements do not always yield improved predictions, especially when markers are correlated or exhibit low specificity [42].

Table 2. Hypercoagulability Biomarkers and Their Prognostic Potential in Preeclampsia

Biomarker	Pathophysiological significance	Prognostic potential	Key limitation
Platelet count	Reflects platelet consumption and haemostatic disturbance	Identifies thrombocytopenia associated with severe disease	Reduced count may occur in other pregnancy-related conditions
Mean platelet volume (MPV)	Indicates platelet size and turnover	Potential marker of platelet activation	Analyzer-dependent; inconsistent predictive evidence
D-dimer	Reflects cross-linked fibrin formation and degradation	May indicate increased coagulation and fibrinolytic activity	Physiologically elevated during pregnancy; low specificity
Fibrinogen	Essential substrate for fibrin formation	Falling levels may indicate consumption or disseminated intravascular coagulation	Normally elevated during pregnancy
Prothrombin time (PT) and activated partial thromboplastin time (aPTT)	Assess selected coagulation pathways	Help identify advanced coagulation abnormalities	Often remain normal despite early hypercoagulability
Thrombin–antithrombin complexes	Reflect in vivo thrombin generation	Potential indicators of coagulation activation	Limited availability and standardized prognostic thresholds
Prothrombin fragment 1+2	Indicates prothrombin activation and thrombin generation	Potential marker of early haemostatic activation	Mainly investigational for preeclampsia prediction
Platelet activation markers	Reflect platelet degranulation and activation	May clarify thrombo-inflammatory mechanisms	Limited assay standardization and clinical validation

Abbreviations: aPTT, activated partial thromboplastin time; MPV, mean platelet volume; PT, prothrombin time.

Integrating biomarkers into a precision-prediction framework

1 From individual biomarkers to multivariable risk assessment

The main opportunity lies in merging complementary biological and clinical data without presuming that each available marker contributes independently. A functional clinical model must incorporate maternal traits, gestational age, and average arterial pressure, past obstetric history, significant comorbidities, placental evaluation, angiogenic markers, and specific signs of hemostatic dysfunction (Table 3).

Table 3. The proposed framework has four interconnected domains:

Domain	Candidate variables	Principal purpose
Clinical risk	Maternal history, blood pressure, symptoms, gestational age	Establish baseline risk and clinical urgency
Placental dysfunction	PlGF, sFlt-1/PlGF ratio, fetal growth, uterine artery Doppler	Assess placental disease and short-term risk
Endothelial injury	Angiogenic imbalance, selected endothelial markers, organ-function tests	Characterize vascular dysfunction and maternal complications
Haemostatic disturbance	Platelet count, coagulation profile, selected fibrin-related markers	Identify haemostatic abnormalities and possible deterioration

This framework represents a suggested clinical-research model, not an established scoring system. It must not be executed with random biomarker weights or unverified thresholds. The key question is whether incorporating endothelial and haemostatic data enhances discrimination, calibration, and clinical decision-making compared to a model based solely on traditional clinical evaluation. Researchers ought to evaluate the effectiveness of models that are clinical-only, angiogenic-enhanced, haemostatic-enhanced, and fully integrated. These comparisons would determine if coagulation biomarkers offer truly novel insights or simply repeat current predictors.

2 Early pregnancy: identifying women at increased risk

Early prediction seeks to recognize high-risk pregnancies prior to the onset of clinical disease. Maternal history, past preeclampsia, chronic hypertension, kidney conditions, diabetes, autoimmune disorders, and various known risk factors continue to be significant. When validated pathways and resources allow, these elements might be integrated with mean arterial pressure, uterine artery Doppler, and PlGF-based evaluation. A crucial action is the prompt start of low-dose aspirin in suitable women, following relevant clinical guidelines and pregnancy timing. Prophylaxis should proceed without delay from biomarker testing when existing clinical criteria justify treatment. The most significant advantage of integrating biomarkers early is better risk categorization: pinpointing women requiring increased monitoring while preventing excessive testing and referrals for those at reduced risk. Nevertheless, screening effectiveness needs to be assessed prospectively, considering false-positive findings, false reassurance, costs, and varied performance among maternal groups [43].

3 Suspected preterm preeclampsia: resolving diagnostic uncertainty

Women exhibiting hypertension, headache, visual disturbances, abdominal discomfort, or unusual lab results may need swift evaluation to differentiate preeclampsia from other conditions and assess the necessity for hospitalization or specialist referral. In this context, testing based on PlGF or the sFlt-1/PlGF ratio could enhance clinical assessments, blood pressure checks, urine analysis, platelet counts, kidney function tests, liver enzyme evaluations, and fetal assessments. A comforting angiogenic outcome can facilitate a reduced projected likelihood of short-term illness in suitably chosen women. On the other hand, an

unusual result might warrant more rigorous monitoring and additional evaluation. No result should take precedence over strong clinical evidence. Severe persistent hypertension, eclampsia, pulmonary edema, worsening thrombocytopenia, liver damage, or fetal distress necessitates proper management irrespective of angiogenic biomarker results [44].

4 Established preeclampsia: predicting progression and complications

After diagnosing preeclampsia, the clinical focus changes from forecasting the onset of the disease to expecting its worsening. Continuous monitoring of blood pressure, symptoms, platelet levels, kidney and liver function, oxygen levels, and fetal evaluations continues to be crucial. Angiogenic imbalance could offer further insights into placental disorders and the chances of negative outcomes, especially in cases of preterm presentations. Abnormalities in haemostasis may indicate patients who need evaluation for consumption, bleeding, thrombosis, or additional complications. The combination may ultimately enhance the recognition of women needing tertiary referral or closer monitoring [45].

Precision-guided maternal–fetal management

Biomarkers are clinically valuable only if their findings guide suitable choices. Their execution should consequently be associated with established management protocols instead of standalone laboratory reporting. Low assessed short-term risk: When clinical evaluation is reassuring and a validated angiogenic test shows low short-term risk, healthcare providers may opt for outpatient monitoring, explicit return instructions, and planned re-evaluation. This method necessitates dependable monitoring and should not be employed when maternal or fetal indications alone justify admission [42]. Moderate or ambiguous risk: Women whose clinical and biomarker results do not align may need ongoing clinical evaluations, laboratory testing, fetal growth monitoring, and Doppler examinations if necessary. Discordance ought to prompt analysis instead of immediate labeling as low- or high-risk. Elevated risk or known complications: Critical hypertension, advancing organ impairment, neurological signs, unusual fetal monitoring, or suspected coagulopathy necessitates immediate intervention and suitable referral. Biomarker findings can enhance evaluation but should not postpone stabilization, antihypertensive therapy, magnesium sulfate when needed, or delivery when clinically required [44].

Implementation challenges in resource-constrained settings

The possible advantages of integrating biomarkers are especially significant in low- and middle-income nations, where the complications from preeclampsia may be exacerbated by late presentation, inadequate laboratory facilities, lack of trained staff, and limited access to full emergency obstetric services. However, advanced biomarker testing might not be accessible or affordable in district hospitals. Conducting costly assays without dependable blood pressure monitoring, urine analysis, emergency referrals, antihypertensive medications, magnesium sulfate, and critical laboratory services will not overcome the main obstacles to survival. An effective implementation plan should emphasize dependable standard assessments, accompanied by selective application of validated angiogenic tests when accessible. Regional laboratories might assist referral networks, and point-of-care platforms may enhance access provided their analytical performance, turnaround times, and costs are satisfactory [46]. Haemostatic testing necessitates careful consideration, as physiological changes associated with pregnancy may result in misinterpretation if non-pregnancy reference intervals are used. Laboratories need to set or confirm suitable reference intervals, standardize the handling of specimens, and ensure that clinicians are aware of the limitations specific to each assay [1]. Equity should be a fundamental criterion for implementation. Models primarily created in high-income groups may not transfer effectively to environments with varying maternal traits, disease rates, comorbid conditions, and healthcare accessibility. External validation must encompass African and other marginalized populations. Assessment should evaluate not just

predictive accuracy but also cost-effectiveness, delays in referrals, accessibility to treatment, and maternal-perinatal results [10].

Conclusion

Predicting preeclampsia necessitates moving beyond dependence on just blood pressure and proteinuria to a comprehensive evaluation of placental dysfunction, endothelial damage, coagulation irregularities, and maternal-fetal condition. Angiogenic biomarkers, especially the PlGF and sFlt-1/PlGF ratio, provide important clinical insights for assessing suspected preterm preeclampsia and enhancing short-term risk evaluation. Certain haemostatic indicators, such as platelet count and coagulation parameters, can enhance this information by detecting the progression of organ dysfunction and coagulopathy. Nonetheless, the additional predictive value of integrating these biomarkers is still not firmly established, and many endothelial and advanced coagulation markers continue to be under investigation. The focus is on creating and confirming clinically useful models that show enhanced predictive accuracy, calibration, and decision-making compared to traditional clinical evaluations. Future multicenter studies ought to set population-relevant thresholds, assess performance over varying gestational ages, and ascertain if biomarker-driven pathways lower avoidable maternal and perinatal complications without escalating unnecessary interventions or iatrogenic prematurity. Implementation must integrate cost-effectiveness, laboratory feasibility, and equitable access, especially in settings with limited resources.

Declarations

Ethics Approval and Consent to Participate: Not applicable. This narrative review did not involve human participants, animal experiments, or the collection of primary data.

Consent for Publication: Not applicable.

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References

1. Chang KJ, Seow KM, Chen KH. Preeclampsia: Recent Advances in Predicting, Preventing, and Managing the Maternal and Fetal Life-Threatening Condition. Int J Environ Res Public Health. 2023;20(4):2994. doi: 10.3390/ijerph20042994.
2. Gathiram P, Moodley J. Pre-eclampsia: its pathogenesis and pathophysiolgy. Cardiovasc J Afr. 2016;27(2):71-8. doi: 10.5830/CVJA-2016-009.
3. Torres-Torres J, Espino-Y-Sosa S, Martinez-Portilla R, Borboa-Olivares H, Estrada-Gutierrez G, Acevedo-Gallegos S, Ruiz-Ramirez E, Velasco-Espin M, Cerda-Flores P, Ramirez-Gonzalez A, Rojas-Zepeda L. A Narrative Review on the Pathophysiology of Preeclampsia. Int J Mol Sci. 2024;25(14):7569. doi: 10.3390/ijms25147569.
4. McElwain CJ, Tuboly E, McCarthy FP, McCarthy CM. Mechanisms of Endothelial Dysfunction in Pre-eclampsia and Gestational Diabetes Mellitus: Windows into Future Cardiometabolic Health? Front Endocrinol (Lausanne). 2020; 11:655. doi: 10.3389/fendo.2020.00655.
5. Sánchez-Aranguren LC, Prada CE, Riaño-Medina CE, Lopez M. Endothelial dysfunction and preeclampsia: role of oxidative stress. Front Physiol. 2014; 5:372. doi: 10.3389/fphys.2014.00372.
6. Kontovazainitis CG, Gialamprinou D, Theodoridis T, Mitsiakos G. Hemostasis in Pre-Eclamptic Women and Their Offspring: Current Knowledge and Hemostasis Assessment with Viscoelastic Tests.

Diagnostics (Basel). 2024;14(3):347. doi: 10.3390/diagnostics14030347.
7. Godtfredsen AC, Sidelmann JJ, Dolleris BB, Jørgensen JS, Johansen EKJ, Pedersen MFB, Palarasah Y, Gram JB. Fibrinolytic Changes in Women with Preeclampsia. ClinApplThrombHemost. 2022; 28:10760296221126172. doi: 10.1177/10760296221126172.
8. Wewers TM, Schulz A, Nolte I, Pavenstädt H, Brand M, Di Marco GS. Circulating Soluble Fms-like Tyrosine Kinase in Renal Diseases Other than Preeclampsia. J Am SocNephrol. 2021;32(8):1853-1863. doi: 10.1681/ASN.2020111579.
9. Ugalde MJ, Caballero A, Martín Fernández M, Tamayo E, de la Varga-Martínez O. Value of the biomarker soluble tyrosine kinase 1 type fms (sFLT-1) in the diagnosis and prognosis of sepsis: a systematic review. Med Clin (Barc). 2024;163(5):224-231. English, Spanish. doi: 10.1016/j.medcli.2024.03.027.
10. Goel A, Rana S. Angiogenic factors in preeclampsia: potential for diagnosis and treatment. CurrOpinNephrolHypertens. 2013;22(6):643-50. doi: 10.1097/MNH.0b013e328365ad98.
11. Tomkiewicz J, Darmochwał-Kolarz DA. Biomarkers for Early Prediction and Management of Preeclampsia: A Comprehensive Review. Med SciMonit. 2024;30: e944104. doi: 10.12659/MSM.944104.
12. Phipps EA, Thadhani R, Benzing T, Karumanchi SA. Pre-eclampsia: pathogenesis, novel diagnostics and therapies. Nat Rev Nephrol. 2019;15(5):275-289. doi: 10.1038/s41581-019-0119-6.
13. Powe CE, Levine RJ, Karumanchi SA. Preeclampsia, a disease of the maternal endothelium: the role of antiangiogenic factors and implications for later cardiovascular disease. Circulation. 2011;123(24):2856-69. doi: 10.1161/CIRCULATIONAHA.109.853127.
14. Opichka MA, Rappelt MW, Gutterman DD, Grobe JL, McIntosh JJ. Vascular Dysfunction in Preeclampsia. Cells. 2021;10(11):3055. doi: 10.3390/cells10113055.
15. Guerby P, Tasta O, Swiader A, Pont F, Bujold E, Parant O, Vayssiere C, Salvayre R, Negre-Salvayre A. Role of oxidative stress in the dysfunction of the placental endothelial nitric oxide synthase in preeclampsia. Redox Biol. 2021; 40:101861. doi: 10.1016/j.redox.2021.101861.
16. Jomova K, Raptova R, Alomar SY, Alwasel SH, Nepovimova E, Kuca K, Valko M. Reactive oxygen species, toxicity, oxidative stress, and antioxidants: chronic diseases and aging. Arch Toxicol. 2023;97(10):2499-2574. doi: 10.1007/s00204-023-03562-9.
17. Harmon AC, Cornelius DC, Amaral LM, Faulkner JL, Cunningham MW Jr, Wallace K, LaMarca B. The role of inflammation in the pathology of preeclampsia. ClinSci (Lond). 2016;130(6):409-19. doi: 10.1042/CS20150702.
18. McElwain CJ, Tuboly E, McCarthy FP, McCarthy CM. Mechanisms of Endothelial Dysfunction in Pre-eclampsia and Gestational Diabetes Mellitus: Windows into Future Cardiometabolic Health? Front Endocrinol (Lausanne). 2020; 11:655. doi: 10.3389/fendo.2020.00655.
19. Su JB. Vascular endothelial dysfunction and pharmacological treatment. World J Cardiol. 2015;7(11):719-41. doi: 10.4330/wjc.v7.i11.719.
20. Blanco-Rivero J, Cachofeiro V, Lahera V, Aras-Lopez R, Márquez-Rodas I, Salaices M, Xavier FE, Ferrer M, Balfagón G. Participation of prostacyclin in endothelial dysfunction induced by aldosterone in normotensive and hypertensive rats. Hypertension. 2005;46(1):107-12. doi: 10.1161/01.HYP.0000171479.36880.17.
21. Tomkiewicz J, Darmochwał-Kolarz DA. Biomarkers for Early Prediction and Management of Preeclampsia: A Comprehensive Review. Med SciMonit. 2024;30: e944104. doi: 10.12659/MSM.944104.
22. MacDonald TM, Walker SP, Hannan NJ, Tong S, Kaitu'u-Lino TJ. Clinical tools and biomarkers to predict preeclampsia. EBioMedicine. 2022; 75:103780. doi: 10.1016/j.ebiom.2021.103780.

23. Maynard SE, Min JY, Merchan J, Lim KH, Li J, Mondal S, Libermann TA, Morgan JP, Sellke FW, Stillman IE, Epstein FH, Sukhatme VP, Karumanchi SA. Excess placental soluble fms-like tyrosine kinase 1 (sFlt1) may contribute to endothelial dysfunction, hypertension, and proteinuria in preeclampsia. J Clin Invest. 2003;111(5):649-58. doi: 10.1172/JCI17189.
24. Jena MK, Sharma NR, Petitt M, Maulik D, Nayak NR. Pathogenesis of Preeclampsia and Therapeutic Approaches Targeting the Placenta. Biomolecules. 2020;10(6):953. doi: 10.3390/biom10060953.
25. Parchem JG, Kanasaki K, Kanasaki M, Sugimoto H, Xie L, Hamano Y, Lee SB, Gattone VH, Parry S, Strauss JF, Garovic VD, McElrath TF, Lu KH, Sibai BM, LeBleu VS, Carmeliet P, Kalluri R. Loss of placental growth factor ameliorates maternal hypertension and preeclampsia in mice. J Clin Invest. 2018;128(11):5008-5017. doi: 10.1172/JCI99026.
26. Albonici L, Benvenuto M, Focaccetti C, Cifaldi L, Miele MT, Limana F, Manzari V, Bei R. PlGF Immunological Impact during Pregnancy. Int J Mol Sci. 2020;21(22):8714. doi: 10.3390/ijms21228714.
27. Granger JP, Spradley FT, Bakrania BA. The Endothelin System: A Critical Player in the Pathophysiology of Preeclampsia. CurrHypertens Rep. 2018;20(4):32. doi: 10.1007/s11906-018-0828-4.
28. Sheppard SJ, Khalil RA. Risk factors and mediators of the vascular dysfunction associated with hypertension in pregnancy. CardiovascHematolDisord Drug Targets. 2010;10(1):33-52. doi: 10.2174/187152910790780096.
29. Sibal L, Agarwal SC, Home PD, Boger RH. The Role of Asymmetric Dimethylarginine (ADMA) in Endothelial Dysfunction and Cardiovascular Disease. CurrCardiol Rev. 2010;6(2):82-90. doi: 10.2174/157340310791162659.
30. Böger RH. Asymmetric dimethylarginine, an endogenous inhibitor of nitric oxide synthase, explains the "L-arginine paradox" and acts as a novel cardiovascular risk factor. J Nutr. 2004;134(10 Suppl):2842S-2847S; discussion 2853S. doi: 10.1093/jn/134.10.2842S. PMID: 15465797.
31. Canbakan B, Keven K, Tutkak H, Danisman N, Ergun I, Nergizoglu G. Circulating endothelial cells in preeclampsia. J Hum Hypertens. 2007;21(7):558-63. doi: 10.1038/sj.jhh.1002199.
32. Mehrabian F, Jazi SM, Javanmard SH, Kaviani M, Homayouni V. Circulating endothelial cells (CECs) and E-selectin: Predictors of preeclampsia. J Res Med Sci. 2012;17(1):15-21.
33. Agarwal I, Karumanchi SA. Preeclampsia and the Anti-Angiogenic State. Pregnancy Hypertens. 2011;1(1):17-21. doi: 10.1016/j.preghy.2010.10.007.
34. Raia-Barjat T, Edebiri O, Ni Ainle F. Preeclampsia and Venous Thromboembolism: Pathophysiology and Potential Therapy. Front Cardiovasc Med. 2022; 9:856923. doi: 10.3389/fcvm.2022.856923.
35. Yoon HJ. Coagulation abnormalities and bleeding in pregnancy: an anesthesiologist's perspective. Anesth Pain Med (Seoul). 2019;14(4):371-379. doi: 10.17085/apm.2019.14.4.371.
36. Siennicka A, Kłysz M, Chełstowski K, Tabaczniuk A, Marcinowska Z, Tarnowska P, Kulesza J, Torbe A, Jastrzębska M. Reference Values of D-Dimers and Fibrinogen in the Course of Physiological Pregnancy: The Potential Impact of Selected Risk Factors-A Pilot Study. Biomed Res Int. 2020; 2020:3192350. doi: 10.1155/2020/3192350.
37. Rodríguez-Peña Y, Ibáñez-Pinilla M. Elevated levels of D-dimer tested by immunoturbidimetry are associated with the extent of severity of pre-eclampsia. Int J Gynaecol Obstet. 2020;150(2):241-247. doi: 10.1002/ijgo.13163.
38. Erez O, Romero R, Hoppensteadt D, Than NG, Fareed J, Mazaki-Tovi S, Espinoza J, Chaiworapongsa T, Kim SS, Yoon BH, Hassan SS, Gotsch F, Friel L, Vaisbuch E, Kusanovic JP. Tissue factor and its natural inhibitor in pre-eclampsia and SGA. J MaternFetal Neonatal Med. 2008;21(12):855-869. doi: 10.1080/14767050802361872.

39. Agbani EO, Skeith L, Lee A. Preeclampsia: Platelet procoagulant membrane dynamics and critical biomarkers. Res PractThrombHaemost. 2023;7(2):100075. doi: 10.1016/j.rpth.2023.100075.
40. Han C, Chen YY, Dong JF. Prothrombotic state associated with preeclampsia. CurrOpinHematol. 2021;28(5):323-330. doi: 10.1097/MOH.0000000000000678.
41. Godtfredsen AC, Sidelmann JJ, Dolleris BB, Jørgensen JS, Johansen EKJ, Pedersen MFB, Palarasah Y, Gram JB. Fibrinolytic Changes in Women with Preeclampsia. ClinApplThrombHemost. 2022; 28:10760296221126172. doi: 10.1177/10760296221126172.
42. Cesari M, Pahor M, Incalzi RA. Plasminogen activator inhibitor-1 (PAI-1): a key factor linking fibrinolysis and age-related subclinical and clinical conditions. CardiovascTher. 2010;28(5): e72-91. doi: 10.1111/j.1755-5922.2010.00171.x.
43. Tomkiewicz J, Darmochwał-Kolarz DA. Biomarkers for Early Prediction and Management of Preeclampsia: A Comprehensive Review. Med SciMonit. 2024;30: e944104. doi: 10.12659/MSM.944104.
44. Velegrakis A, Kouvidi E, Fragkiadaki P, Sifakis S. Predictive value of the sFlt-1/PlGF ratio in women with suspected preeclampsia: An update (Review). Int J Mol Med. 2023;52(4):89. doi: 10.3892/ijmm.2023.5292.
45. Rybak-Krzyszkowska M, Staniczek J, Kondracka A, Bogusławska J, Kwiatkowski S, Góra T, Strus M, Górczewski W. From Biomarkers to the Molecular Mechanism of Preeclampsia-A Comprehensive Literature Review. Int J Mol Sci. 2023;24(17):13252. doi: 10.3390/ijms241713252.
46. Wada H, Shiraki K, Shimpo H, Shimaoka M, Iba T, Suzuki-Inoue K. Thrombotic Mechanism Involving Platelet Activation, Hypercoagulability and Hypofibrinolysis in Coronavirus Disease 2019. Int J Mol Sci. 2023;24(9):7975. doi: 10.3390/ijms24097975.

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