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# PREDICTION OF PREECLAMPSIA DEVELOPMENT IN PREGNANT WOMEN WITH OVERWEIGHT AND OBESITY

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**Abstract**
This review evaluates current predictive models and biomarkers for preeclampsia in overweight and obese pregnant women, focusing on their clinical effectiveness and practical application. Maternal obesity is linked to preeclampsia through mechanisms such as chronic inflammation, endothelial dysfunction, and abnormal placental development. Advances in biomarkers like placental growth factor, soluble fms-like tyrosine kinase-1, and metabolomic profiles have improved early detection, though predictive accuracy varies with body mass index. Machine learning models combining biomarkers and maternal data outperform traditional methods. Effective clinical use requires attention to cost, resources, and healthcare infrastructure. The review offers evidence-based recommendations to enhance preeclampsia prediction in high-risk obese pregnancies, highlighting the importance of personalized and integrated care strategies.

**Keywords**: preeclampsia, obesity, pregnancy, biomarkers, prediction models, maternal health, placental growth factor, risk assessment

## Introduction

Today, preeclampsia continues to represent one of the most formidable challenges in modern obstetric care, affecting approximately 2-8% of pregnancies worldwide and serving as a leading cause of maternal and perinatal morbidity and mortality. The condition accounts for approximately 14% of maternal deaths and 10-25% of perinatal deaths globally, while also attracting attention for its association with risks for developing chronic diseases in later life for both mother and child. The escalating global obesity epidemic has introduced additional complexity to this clinical landscape, with overweight and obese women demonstrating 1.92-fold and 5.06-fold increased risks for preeclampsia development, respectively, compared to women with normal body mass index.

The intersection of maternal obesity and preeclampsia development presents unique challenges for healthcare providers, requiring sophisticated understanding of underlying pathophysiological mechanisms and advanced predictive approaches. Traditional risk assessment methods often prove inadequate for accurately identifying high-risk obese pregnant women, necessitating the development of more refined screening strategies that account for the complex interplay between metabolic dysfunction, inflammatory processes, and placental development abnormalities characteristic of this population. Recent technological advances in biomarker identification,



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genomic analysis, and artificial intelligence applications have opened new avenues for improving preeclampsia prediction accuracy in obese pregnancies. However, the translation of these innovations into clinical practice requires careful evaluation of their effectiveness, feasibility, and integration with existing healthcare systems. The development of evidence-based prediction models specifically designed for overweight and obese pregnant women represents a critical step toward reducing the burden of preeclampsia-related complications and improving maternal and fetal outcomes.

**Main Part**

The relationship between maternal obesity and preeclampsia development involves intricate pathophysiological mechanisms that extend beyond simple hemodynamic alterations. Obesity is considered a risk factor for preeclampsia with many common mechanisms linking obesity with higher risk of developing preeclampsia, while both conditions share associations with increased risk of future cardiovascular diseases. These shared pathways provide important insights into disease prediction and intervention opportunities. Chronic low-grade inflammation represents a fundamental characteristic of both obesity and preeclampsia, creating a synergistic environment that promotes disease progression. Adipose tissue in obese individuals produces elevated levels of pro-inflammatory cytokines, including tumor necrosis factor-alpha, interleukin-6, and C-reactive protein, which contribute to systemic inflammatory responses. This inflammatory milieu interferes with normal placental development and vascular adaptation processes essential for healthy pregnancy outcomes.

Endothelial dysfunction serves as another critical mechanistic link between obesity and preeclampsia development. Excessive adipose tissue accumulation leads to altered production of vasoactive substances, including reduced nitric oxide bioavailability and increased production of vasoconstrictor agents. These changes compromise maternal vascular adaptation to pregnancy, reducing placental perfusion and contributing to the characteristic hypertensive and proteinuric manifestations of preeclampsia. The placental interface represents a particularly vulnerable site where obesity-related metabolic alterations exert significant influence on pregnancy outcomes. Maternal obesity affects placental development through multiple mechanisms, including altered angiogenesis, impaired trophoblast invasion, and modified maternal-fetal nutrient transport. These changes result in placental hypoxia and oxidative stress, triggering the release of anti-angiogenic factors that contribute to the systemic manifestations of preeclampsia. Insulin resistance, a hallmark of obesity, further complicates the pathophysiological landscape by promoting hyperinsulinemia and altered glucose metabolism. These metabolic disturbances affect placental function and contribute to the development of gestational diabetes mellitus, which frequently coexists with preeclampsia in obese pregnant women. The interconnected nature of these metabolic disorders necessitates comprehensive risk assessment approaches that consider multiple pathophysiological pathways simultaneously.

The identification and validation of reliable biomarkers for preeclampsia prediction in obese pregnant women has emerged as a critical research priority, with significant advances achieved in recent years. Recent systematic reviews have revealed that 77% of prediction models combine biomarkers with maternal clinical characteristics, with pregnancy-associated plasma protein-A and



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placental growth factor serving as the most frequently utilized predictive markers. Placental growth factor has demonstrated particular promise as a predictive biomarker, reflecting its central role in placental angiogenesis and vascular development. Decreased placental growth factor levels during early pregnancy correlate strongly with subsequent preeclampsia development, particularly in high-risk populations including obese women. The biomarker demonstrates enhanced predictive value when combined with other angiogenic factors and clinical parameters, providing improved risk stratification capabilities. Soluble fms-like tyrosine kinase-1 represents another critical component of the angiogenic biomarker panel, serving as an anti-angiogenic factor that increases significantly prior to clinical preeclampsia manifestation. These biomarkers are now being used clinically in cases of suspected preterm preeclampsia, with their high negative predictive value enabling confident exclusion of disease in women with normal results, although sensitivity remains modest. The ratio of soluble fms-like tyrosine kinase-1 to placental growth factor has shown superior predictive performance compared to individual marker assessment. Metabolomic profiling has emerged as a promising avenue for improving prediction accuracy, particularly in obese populations where traditional biomarkers may demonstrate reduced effectiveness. Single metabolites and ratios of amino acids related to arginine bioavailability and nitric oxide synthase pathways have been associated with preterm preeclampsia risk at 11 to 13 weeks of gestation, with differential prediction observed according to body mass index classes. This finding supports the existence of distinct pathophysiological pathways in different weight categories, necessitating tailored biomarker approaches. Novel biomarker categories, including cell-free DNA, microRNA profiles, and proteomic signatures, have shown preliminary promise for enhancing prediction accuracy. Routinely available patient characteristics combined with cell-free DNA markers can predict preeclampsia with performance comparable to other patient characteristic models for preterm preeclampsia prediction. These emerging biomarkers offer potential advantages including non-invasive sampling methods and early detection capabilities.

The integration of multiple biomarker categories through advanced analytical approaches has demonstrated superior predictive performance compared to single-marker strategies. Metabolite biomarkers can be combined with established biomarkers of placental growth factor, mean arterial pressure, and uterine artery pulsatility index to improve the biomarker component of early-pregnancy preterm preeclampsia prediction tests. This multiparameter approach addresses the complex and heterogeneous nature of preeclampsia pathophysiology.

The development of sophisticated prediction models incorporating multiple risk factors, biomarkers, and clinical parameters represents a significant advancement in preeclampsia risk assessment for obese pregnant women. Machine learning approaches and artificial intelligence applications have shown particular promise for improving prediction accuracy and enabling more precise risk stratification. Traditional prediction models based solely on clinical risk factors have demonstrated limited effectiveness in obese populations, where conventional risk assessment tools often underestimate disease probability. The complexity of obesity-related pathophysiological mechanisms requires more sophisticated analytical approaches capable of processing multiple variables simultaneously and identifying non-linear relationships between predictive factors. Machine learning algorithms, including logistic regression, neural networks, and ensemble methods, have shown superior performance compared to traditional statistical approaches. These



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algorithms can effectively integrate diverse data types, including clinical parameters, biomarker profiles, imaging findings, and demographic characteristics, to generate comprehensive risk assessments. The ability to continuously learn and adapt from new data enables these models to improve prediction accuracy over time.

Artificial intelligence applications have demonstrated particular strength in identifying subtle patterns and relationships within complex datasets that may not be apparent through conventional analysis methods. Deep learning approaches can process high-dimensional biomarker data, including genomic, proteomic, and metabolomic profiles, to extract predictive features that enhance risk assessment accuracy. These capabilities are particularly valuable for obese populations where traditional risk factors may demonstrate altered predictive relationships. The implementation of prediction models requires careful consideration of clinical workflow integration and healthcare provider training requirements. User-friendly interfaces and automated risk calculation systems can facilitate model adoption while maintaining accuracy and reliability. However, the complexity of advanced prediction algorithms necessitates robust validation studies and ongoing performance monitoring to ensure continued effectiveness across diverse patient populations. External validation studies across different geographic regions and healthcare settings have demonstrated variable model performance, highlighting the importance of local adaptation and calibration processes. Population-specific factors, including genetic backgrounds, environmental exposures, and healthcare delivery systems, may influence model accuracy and require customization for optimal performance.

The successful translation of advanced preeclampsia prediction models into routine clinical practice requires comprehensive implementation strategies that address technical, educational, and organizational challenges. Healthcare systems must develop integrated approaches that incorporate prediction tools into existing prenatal care workflows while ensuring adequate provider training and patient education. Resource allocation considerations play a critical role in determining the feasibility of implementing sophisticated prediction models, particularly in healthcare settings with limited laboratory capabilities or technological infrastructure. Cost-effectiveness analyses must evaluate the economic impact of enhanced screening programs compared to standard care approaches, considering both immediate implementation costs and long-term savings from improved maternal and fetal outcomes. The timing of prediction model application represents a crucial implementation consideration, with early pregnancy screening offering optimal intervention opportunities but requiring careful balance between sensitivity and specificity to avoid unnecessary anxiety and interventions. First-trimester screening protocols must be designed to maximize detection rates while minimizing false-positive results that could lead to inappropriate clinical management.

Provider education programs must address the interpretation and clinical application of prediction model results, ensuring that healthcare professionals understand the limitations and appropriate use of these tools. Training curricula should emphasize the integration of prediction results with clinical judgment and the importance of individualized patient care approaches that consider the complete clinical picture. Patient counseling protocols require development to effectively communicate prediction results and associated recommendations to pregnant women and their families. Educational materials must present complex risk information in accessible formats while



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promoting informed decision-making and adherence to recommended interventions. Cultural sensitivity and language accessibility considerations are essential for effective patient communication. Quality assurance programs must be established to monitor prediction model performance and ensure continued accuracy over time. Regular calibration studies, outcome tracking, and model updating processes are necessary to maintain optimal predictive performance as patient populations and clinical practices evolve.

The future of preeclampsia prediction in obese pregnant women lies in the continued development of personalized medicine approaches that integrate multiple data sources to provide individualized risk assessments and intervention strategies. Advances in genomic medicine, including genome-wide association studies and polygenic risk scores, offer potential for incorporating genetic susceptibility factors into comprehensive prediction models. Emerging technologies, including wearable monitoring devices and remote sensing capabilities, may enable continuous risk assessment throughout pregnancy rather than relying solely on discrete clinical encounters. These approaches could provide real-time monitoring of physiological parameters and early detection of concerning changes that precede clinical preeclampsia manifestation. The integration of social determinants of health into prediction models represents an important frontier for improving risk assessment accuracy and addressing health disparities. Factors including socioeconomic status, access to healthcare, nutritional status, and environmental exposures may significantly influence preeclampsia risk and require incorporation into comprehensive prediction frameworks. Collaborative research initiatives and data sharing platforms will be essential for advancing prediction model development and validation across diverse populations. International consortiums and standardized data collection protocols can facilitate the development of robust prediction tools that demonstrate effectiveness across different healthcare settings and patient populations.

In conclusion, Predicting preeclampsia in pregnant women with overweight and obesity is a complex clinical challenge that requires advanced biomarkers, clinical data, and innovative analytical methods. Obese women are at higher risk, necessitating tailored screening strategies. Combining biomarkers like angiogenic factors and metabolomic profiles with machine learning improves prediction accuracy. However, successful implementation depends on healthcare system readiness, provider training, and equitable access. Future research should prioritize personalized approaches that consider individual and social risk factors. Advancements in prediction technologies and deeper understanding of obesity-related mechanisms offer potential to reduce preeclampsia risk and improve outcomes.

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