INTERNATIONAL JOURNAL OF CURRENT RESEARCH IN CHEMISTRY AND PHARMACEUTICAL SCIENCES
(p-ISSN: 2348-5213: e-ISSN: 2348-5221)
www.ijcrcps.com
(A Peer Reviewed, Referred, Indexed and Open Access Journal)
DOI: 10.22192/ijcrcps Coden: IJCROO(USA) Volume 12, Issue 9- 2025

Review Article

DOI: http://dx.doi.org/10.22192/ijcrcps.2025.12.09.003

Platelet Indices as Predictors of Adverse Pregnancy Outcomes in Aged Women: A Narrative Review

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Abstract

Pregnancy at advanced maternal age (AMA) is increasingly common and is accompanied by heightened risks of obstetric complications, including preeclampsia, gestational hypertension, recurrent miscarriage, preterm birth, and intrauterine growth restriction. Hematologic adaptations during pregnancy are further influenced by age-related endothelial dysfunction, inflammation, and altered platelet biology. Platelet indices—such as mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), and platelet count—have emerged as simple, cost-effective biomarkers that may aid in predicting adverse maternal and fetal outcomes. Evidence suggests that elevated MPV and PDW are associated with preeclampsia and placental insufficiency, while low platelet counts and PCT values may indicate severe disease progression. This narrative review summarizes the biological rationale for platelet alterations in AMA pregnancies, evaluates their clinical utility as predictive tools, and highlights limitations and research gaps. Establishing standardized thresholds and integrating platelet indices into predictive models could enhance early risk stratification and improve maternal–fetal care in older pregnant women.

Keywords: Platelet indices, Advanced maternal age, Pregnancy outcomes, Preeclampsia, Hematology

Introduction

Pregnancy at advanced maternal age (AMA), typically defined as conception at or beyond 35 years, has become increasingly prevalent worldwide as women delay childbearing due to career pursuits, socioeconomic factors, or reliance on assisted reproductive technologies. While improvements in obstetric care have expanded reproductive opportunities for older women, AMA pregnancies are consistently associated with heightened maternal and fetal risks. These include hypertensive disorders of pregnancy, recurrent miscarriage, preterm delivery, intrauterine growth restriction, and stillbirth. Such complications underscore the importance of identifying early and reliable predictors of adverse outcomes in this vulnerable population [1].Physiological changes during pregnancy already impose significant hematologic demands, with adaptations in coagulation, platelet dynamics, and vascular function aimed at sustaining maternal health and placental circulation. In AMA women, however, these adaptations intersect with age-related vascular stiffening, hormonal decline, and immune dysregulation, thereby compounding the risk of hematologic imbalance. As a result, routine monitoring parameters that reflect both maternal physiology and placental health have gained attention as potential predictive tools [2-3].

Platelets, long recognized for their role in hemostasis, are now understood as active participants in inflammation, angiogenesis, and vascular homeostasis. During pregnancy, platelet activation is critical for placental implantation and development. Yet excessive or dysregulated platelet activation can impair uteroplacental blood flow and contribute to microthrombi formation, endothelial dysfunction, and placental insufficiency—key mechanisms underlying adverse pregnancy outcomes, particularly in AMA women [4-5].In this context, platelet indices derived from routine complete blood counts (CBCs) have emerged as valuable, cost-effective biomarkers. Parameters such as mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), and platelet count offer indirect but sensitive insights into platelet production, activation, and consumption. Unlike specialized biomarkers that require advanced assays, platelet indices are universally available in clinical practice, making them practical candidates for widespread application in risk stratification [6-7].

Emerging evidence links altered platelet indices with specific complications in AMA pregnancies. Elevated MPV and PDW have been associated with preeclampsia and gestational hypertension, conditions marked by endothelial activation and platelet hyperactivity. Reduced platelet count and low PCT values, on the other hand, may signal disease progression toward severe preeclampsia or HELLP syndrome. Furthermore, platelet indices have been implicated in predicting miscarriage, intrauterine growth restriction, and preterm birth, highlighting their potential as multipurpose markers of maternal–fetal compromise [8-9].Despite their promise, several challenges limit the clinical application of platelet indices. Variations in reference ranges across laboratories, lack of standardized cut-off thresholds, and confounding influences from comorbidities such as diabetes and obesity complicate interpretation. Additionally, relatively few studies have focused specifically on AMA pregnancies, leaving important gaps in our understanding of how platelet dynamics in this group differ from younger gravidas. Addressing these gaps is crucial for translating platelet indices into effective tools for clinical decision-making [10-11].

Biological Rationale for Platelet Alterations in Advanced Maternal Age

Pregnancy is accompanied by profound hematologic and vascular adaptations designed to support placental perfusion and fetal growth. These include a shift toward hypercoagulability, accelerated platelet turnover, and enhanced endothelial activity. In women of advanced maternal age (AMA), however, the physiological demands of pregnancy intersect with age-related changes in the vascular and hematopoietic

systems, producing distinctive alterations in platelet function and indices [12-13].One of the central contributors is endothelial dysfunction, a hallmark of vascular aging. Reduced vascular elasticity and diminished nitric oxide bioavailability enhance platelet activation and aggregation, leading to increases in mean platelet volume (MPV) and platelet distribution width (PDW). These changes are further amplified by chronic low-grade inflammation and oxidative stress, commonly referred to as "inflammaging." Persistent systemic inflammation accelerates platelet consumption and turnover, resulting in greater variability in platelet size and function [14].

Bone marrow aging also plays a role, as senescent hematopoietic stem cells exhibit reduced efficiency in megakaryopoiesis. This decline may manifest as lower platelet counts or fluctuations in plateletcrit (PCT), particularly in women with coexisting metabolic disorders such as diabetes and hypertension. In addition, the placenta in AMA pregnancies often shows maladaptive changes, including inadequate trophoblast invasion and impaired spiral artery remodeling. These processes contribute to placental hypoperfusion and microthrombus formation at the maternal–fetal interface, both of which stimulate platelet activation and release of pro-inflammatory mediators.

Metabolic and hormonal influences add another layer of complexity. Older women are more likely to have obesity, metabolic syndrome, or altered estrogen and progesterone dynamics, all of which can intensify platelet activation and disrupt hemostatic balance [15].

Platelet Indices in Predicting Adverse Pregnancy Outcomes

Platelet indices have gained recognition as useful indicators of maternal vascular and hematologic status during pregnancy. Among these, mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), and platelet count provide valuable insights into platelet activation, heterogeneity, and overall production. In women of advanced maternal age (AMA), these indices become even more relevant as they may help identify pregnancies at risk of complications that arise from impaired placental function, endothelial dysfunction, and maternal comorbidities [16].One of the most studied complications in relation to platelet indices is preeclampsia and other hypertensive disorders of pregnancy. Elevated MPV and PDW have been consistently reported in women who develop preeclampsia, reflecting increased platelet activation and heterogeneity in size distribution. Larger platelets are metabolically more active and release greater amounts of prothrombotic and vasoactive mediators, thereby exacerbating vascular dysfunction. In severe cases, declining platelet count and reduced PCT further signal progression toward complications such as HELLP syndrome, which is particularly concerning in older pregnant women who already have diminished vascular resilience [17].

Platelet indices have also been implicated in the risk of miscarriage and recurrent pregnancy loss. In AMA women, platelet hyperactivity can contribute to placental microthrombosis and impaired trophoblast invasion, both of which compromise early implantation. Elevated MPV has been observed in women with recurrent miscarriages, suggesting that larger, hyperactive platelets may predispose to early pregnancy failure. These findings underscore the potential of platelet indices as accessible markers for identifying women at risk of early pregnancy loss, especially in populations where age-related vascular and immune changes are already present [18].In addition, platelet indices provide important clues in cases of preterm birth and intrauterine growth restriction (IUGR). Elevated PDW, which reflects increased variability in platelet size, has been linked to placental insufficiency, a key driver of growth restriction and premature delivery. In AMA pregnancies, where placental vascular remodeling is often suboptimal, such platelet abnormalities may serve as early indicators of impending complications. Monitoring platelet indices throughout gestation could therefore facilitate timely interventions such

as enhanced fetal surveillance or prophylactic therapy [19].

Although less extensively studied, platelet indices may also play a role in gestational diabetes mellitus (GDM), a condition more common in AMA women. Metabolic dysregulation and insulin resistance contribute to heightened platelet reactivity, which in turn may increase vascular complications for both mother and fetus. Altered MPV and PDW values in women with GDM highlight the interplay between metabolic and hematologic factors, suggesting a broader predictive role for platelet indices beyond hypertensive disorders [20].The clinical value of these indices lies in their practicality and accessibility. Derived from routine complete blood counts, they are cost-effective and universally available, making them suitable even in resource-limited settings. Unlike more specialized biomarkers, platelet indices can be repeatedly monitored across pregnancy to capture dynamic changes in maternal hematology. When interpreted in conjunction with clinical risk factors, they may enhance predictive accuracy and support individualized management strategies for older pregnant women [21].

Clinical Applications and Implications

The clinical utility of platelet indices in pregnancies at advanced maternal age lies in their ability to provide a simple, inexpensive, and widely available means of identifying women at increased risk of complications. Unlike specialized biomarkers or genetic tests, platelet indices can be obtained from routine complete blood counts, a test that is already a standard component of antenatal care. This accessibility makes them particularly valuable for use in both high-resource and resource-limited settings, where cost and availability often limit the use of advanced diagnostic tools [22].In practice, platelet indices can complement existing risk assessment strategies in AMA pregnancies. For example, an elevated mean platelet volume (MPV) or platelet distribution width (PDW) early in pregnancy may flag a woman at risk of developing preeclampsia, prompting closer blood pressure monitoring, earlier initiation of prophylactic low-dose aspirin, or more frequent antenatal visits. Similarly, declining platelet counts or reduced plateletcrit (PCT) values may alert clinicians to disease progression, thereby guiding timely interventions to prevent severe maternal and fetal morbidity [23].

Beyond hypertensive disorders, platelet indices may also serve as supportive markers in women with recurrent pregnancy loss, intrauterine growth restriction, or preterm labor. Their dynamic nature allows for longitudinal monitoring, enabling clinicians to track changes across trimesters and adjust surveillance intensity accordingly. For instance, a progressive rise in PDW could suggest worsening placental function, warranting Doppler ultrasound evaluation or enhanced fetal monitoring. In this way, platelet indices could contribute to early detection of complications and more personalized care pathways [24].The implications extend to multidisciplinary care as well. For obstetricians, hematologists, and maternal-fetal medicine specialists, integrating platelet indices into clinical algorithms may improve decision-making regarding pharmacological interventions, timing of delivery, and neonatal preparedness. In public health contexts, where the burden of AMA pregnancies is increasing, these indices could be incorporated into population-level screening strategies, improving risk stratification and resource allocation [25].Nevertheless, the translation of platelet indices into clinical practice is not without challenges. Variability in laboratory measurements, the influence of coexisting maternal conditions such as obesity and diabetes, and the lack of standardized reference ranges limit their universal application. Without established thresholds, their predictive power may be underutilized or misinterpreted. Thus, while promising, their clinical role must be viewed as complementary rather than standalone, pending validation in large, prospective studies focused specifically on AMA populations [26].

Conclusion

Pregnancy at advanced maternal age remains a significant clinical challenge due to the heightened risk of maternal and fetal complications. Platelet indices, including mean platelet volume, platelet distribution width, plateletcrit, and platelet count, provide valuable insights into the hematologic and vascular dynamics that underpin these risks. Their ability to reflect platelet activation, turnover, and placental function makes them promising, non-invasive biomarkers for predicting adverse pregnancy outcomes such as preeclampsia, recurrent miscarriage, intrauterine growth restriction, and preterm birth.

As simple and cost-effective parameters obtained from routine complete blood counts, platelet indices are uniquely positioned for integration into antenatal care, particularly in resource-limited settings where advanced biomarkers may be unavailable. However, the absence of standardized thresholds, the influence of comorbidities, and variability in laboratory measurements remain barriers to their widespread adoption.Future research should focus on validating platelet indices in large, prospective studies of advanced maternal age pregnancies, establishing reference ranges, and exploring their integration into risk-prediction models alongside clinical and biochemical markers. With further refinement, platelet indices hold the potential to enhance early risk stratification, guide tailored interventions, and ultimately improve maternal and neonatal outcomes in this growing patient population.

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Quick Response Code

DOI: 10.22192/ijcrcps.2025.12.09.003

How to cite this article:
Emmanuel Ifeanyi Obeagu. (2025). Platelet Indices as Predictors of Adverse Pregnancy Outcomes in Aged Women: A Narrative Review. Int. J. Curr. Res. Chem. Pharm. Sci. 12(9): 52-58.
DOI: http://dx.doi.org/10.22192/ijcrcps.2025.12.09.003

