ICON Journal of Applied Medical Sciences
Volume 01 | Issue 01 | 2025
Journal homepage: https://iconpublishers.com/icon-j-app-med-sci/

DOI: 10.5281/zenodo.17276394

Research Article

Erythrocyte Alterations in Gestational Hypertension: Pathophysiology, Laboratory Perspectives, and Clinical Implications

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Received Date: 24 June 2025

Published Date: 30 Aug. 2025

Abstract

Gestational hypertension (GH) is a pregnancy-specific condition marked by the emergence of hypertension after 20 weeks of gestation in women who were previously normotensive, presenting significant hazards to both maternal and foetal health. In addition to endothelial dysfunction and vascular maladaptation, increasing data indicates that abnormalities in erythrocytes (red blood cells, RBCs) are pivotal in the pathogenesis of pregnant hypertension. Alterations in erythrocyte deformability, oxidative stress, membrane integrity, and hemorheological characteristics lead to compromised microcirculatory perfusion and oxygen delivery, exacerbating placental hypoxia and systemic consequences. This review examines the molecular and cellular mechanisms responsible for erythrocyte modifications in gestational hypertension, focussing on laboratory results, indicators of oxidative damage, and diagnostic methodologies. It also looks at how these alterations could affect maternal-fetal outcomes in a clinical setting and suggests possible therapeutic and research options.

Keywords: Gestational hypertension, erythrocyte deformability, oxidative stress, pregnancy, preeclampsia, red blood cell indices.

Introduction

Gestational hypertension (GH) is a prevalent hypertensive disease in pregnancy, impacting around 6–8% of pregnancies globally. It is characterised by the emergence of hypertension beyond 20 weeks of gestation in a woman who was previously normotensive, without associated proteinuria or end-organ damage. Gestational hypertension is different from preeclampsia, but if it isn't watched and treated properly, it could lead to more serious hypertensive illnesses like preeclampsia or eclampsia [1]. The aetiology of gestational hypertension (GH) is intricate and multifaceted, encompassing vascular, placental, and haematological alterations. Traditionally, the condition has been ascribed mainly to endothelial dysfunction and irregular placental perfusion. Recent research has underscored that modifications in erythrocytes significantly and autonomously contribute to the illness process, affecting blood rheology, oxygen transport, and oxidative equilibrium [2].

Erythrocytes are essential for microcirculatory activity, oxygen transport, and the preservation of redox equilibrium. Changes in the structure or biochemistry of red blood cells can have serious effects on the whole body, especially during pregnancy when the need for oxygen and blood flow is much higher. For red blood cells (RBCs) to be able to travel through capillaries that are smaller than their diameter, they must be strong and flexible. This is important for getting enough oxygen to the mother's tissues and the developing foetus [3]. In gestational hypertension, erythrocytes experience oxidative, structural, and mechanical alterations that impair these functions.Comprehending the characteristics and consequences of these modifications yields significant insights into the underlying mechanisms of GH and presents prospective diagnostic and treatment pathways [4].

The cause of gestational hypertension

Gestational hypertension is caused by problems with the formation of the placenta, problems with the endothelium, problems with the immune system, and increased oxidative stress. In the early stages of pregnancy, the typical process of placental formation entails the infiltration of maternal spiral arteries by trophoblastic cells, transforming them into low-resistance channels capable of facilitating sufficient blood flow to the placenta [5]. In gestational hypertension (GH), this remodeling process is not finished, which causes uteroplacental hypoperfusion and ischaemia. The hypoxic placenta secretes anti-angiogenic and inflammatory mediators, including soluble fms-like tyrosine kinase-1 (sFlt-1) and endoglin, which disseminate systemically and provoke endothelial dysfunction. Endothelial cells under oxidative and inflammatory stress produce less nitric oxide (NO) and prostacyclin, while releasing larger levels of endothelin-1 and thromboxane A2. This imbalance causes the blood vessels to narrow, blood pressure to rise, and platelets to become active. At the same time, it also changes the characteristics of red blood cells by raising oxidative stress, changing the composition of the membrane, and making them less flexible [6].

Oxidative stress is a key part of the chain of events that connects placental hypoxia to damage to red blood cells and blood vessels. Reactive oxygen species (ROS) produced by ischemia–reperfusion damage target membrane lipids, proteins, and DNA. Erythrocytes, which do not have nuclei or mitochondria, rely on enzymatic systems like as superoxide dismutase (SOD), catalase, and glutathione peroxidase, as well as non-enzymatic antioxidants such reduced glutathione (GSH) for their antioxidant defence [7]. These mechanisms are not working properly in gestational hypertension. This leads to the buildup of oxidative chemicals like malondialdehyde (MDA), which is a sign of lipid peroxidation. As a result, the membrane becomes less fluid, the proteins in the cytoskeleton become cross-linked, and red blood cells lose their typical biconcave shape and elasticity [8].

Changes in Erythrocytes During Gestational Hypertension

Microscopic and ultrastructural examinations of erythrocytes in GH often demonstrate atypical morphologies, including echinocytes, spherocytes, and stomatocytes. These morphological alterations signify the rupture of membrane lipid asymmetry and the oxidation of integral proteins, including spectrin, ankyrin, and band. Lipid peroxidation changes the ratio of cholesterol to phospholipids, which makes the cell membrane even less stable and stiffer. Reduced deformability makes it harder for red blood cells to get through capillaries, which makes blood thicker and makes it harder for tissues to get oxygen. These alterations worsen placental and systemic hypoxia, establishing a self-perpetuating cycle of oxidative stress and vascular damage [9].

Another thing that changes in gestational hypertension is erythrocyte osmotic fragility. Increased fragility signifies a diminished capacity of the red cell membrane to endure osmotic stress, frequently attributed to lipid oxidation and impaired functionality of membrane ion pumps, including Na^+/K^+-ATPase and Ca^{2+}-ATPase. The total impact is early death of red blood cells, which could lead to anaemia, but mild hemoconcentration is more common since plasma volume decreases in pregnancies with high blood pressure [10]. Haemoglobin function may potentially be impacted in addition to structural alterations. Oxidative stress can cause haemoglobin to oxidise and lower the levels of 2,3-bisphosphoglycerate (2,3-BPG), which makes it harder for oxygen to get to the tissues of the mother and foetus. In extreme oxidative conditions, increased concentrations of methemoglobin an oxidised, non-functional variant of hemoglobin—may be detected, further hindering oxygen transport [11].

Routine haematological findings

These changes in red blood cells show up in a number of lab tests. Routine haematological tests may show a slight increase in hemoconcentration, a raised haematocrit, and a higher red blood cell count. The mean corpuscular haemoglobin concentration (MCHC) may be somewhat lower, and the red cell distribution width (RDW) is often higher, which shows that the red blood cells are not the same size and shape. Microcytosis or poikilocytosis may be noticed intermittently. These findings, albeit not specific, indicate persistent erythrocyte stress or abnormalities in turnover [12].

Advanced Erythrocyte Function Tests:

Ektacytometry measures how easily red blood cells change shape, and flow cytometry looks for signs of oxidative damage, like ROS inside cells and phosphatidylserine moving outside of cells. Spectrophotometric assays can quantify antioxidant enzyme activity, such as superoxide dismutase (SOD), catalase, and glutathione peroxidase, in addition to oxidative indicators such malondialdehyde (MDA). The osmotic fragility test is still a basic but useful way to determine how stable a membrane is [13]. Biochemical investigations of erythrocyte membranes frequently demonstrate modified phospholipid composition, characterised by reduced unsaturated fatty acids, and protein breakdown, particularly of spectrin and band 3, which may be identified using SDS-PAGE [14].

These laboratory markers together produce a biochemical fingerprint of the stress on red blood cells in pregnancy hypertension. MDA levels are usually high, while the activities of GSH, SOD, and catalase are low. The availability of nitric oxide, which is important for vasodilation, is also lower, which shows that endothelial–erythrocyte crosstalk is not

working properly. These changes can help tell the difference between gestational hypertension and normal pregnancies, and they may be useful for forecasting the progression to preeclampsia [15]. The interaction between erythrocytes and endothelial cells is an important part of keeping blood vessels healthy. Healthy red blood cells can change the tone of blood vessels by moving and releasing nitric oxide. But oxidised or stiff red blood cells pick up NO instead of sending it, which makes blood vessels constrict and keeps high blood pressure going. Additionally, microparticles originating from erythrocytes minute vesicles released after oxidative or mechanical stress can stimulate the endothelium and enhance inflammatory responses. Consequently, erythrocyte malfunction not only signifies but also exacerbates vascular disease in pregnant hypertension [16].

These changes lead to higher vascular resistance and slower microcirculatory flow on a mechanistic level. Stiffened erythrocytes heighten shear stress on artery walls, prompting more endothelial activation and the release of inflammatory cytokines. Placental hypoxia exacerbates oxidative stress and facilitates the release of anti-angiogenic molecules such as sFlt-1, establishing a detrimental cycle that perpetuates hypertension and tissue hypoxia [17]. clinical ramifications of erythrocyte modifications in gestational hypertension The clinical ramifications of erythrocyte modifications in gestational hypertension are substantial. From a diagnostic perspective, haematological and oxidative stress markers may function as preliminary indicators of illness development or progression [18]. Keeping an eye on things like MDA, antioxidant enzyme activity, and red cell deformability may assist figure out who is at danger and what kind of treatment to give them. Moreover, these biomarkers may facilitate the differentiation of pregnant hypertension from preeclampsia, which frequently presents with analogous clinical characteristics however varies in severity and systemic involvement [19]. Antioxidant supplementation has been investigated as a potential therapeutic approach to alleviate oxidative erythrocyte damage in hypertensive pregnancies. Vitamins C and E, N-acetylcysteine, and dietary antioxidants have been investigated, although clinical outcomes continue to exhibit variability. Getting enough micronutrients like zinc, selenium, and copper, which are important cofactors for antioxidant enzymes, may also help keep red blood cells healthy. Nonetheless, excessive antioxidant supplementation should be undertaken with caution, since it may interfere with natural redox signalling [20]. Erythrocyte malfunction in the mother can significantly impact the foetus. Impaired oxygen delivery increases the risk of intrauterine growth restriction (IUGR), premature birth, and low birth weight. Recognising erythrocyte-related problems early on and taking action quickly by the mother can enhance the health of the baby and mother during and after birth. In severe instances, ongoing erythrocyte and endothelial damage may lead to HELLP syndrome, which is characterised by haemolysis, increased liver enzymes, and a diminished platelet count, indicating a critical manifestation of the hypertensive spectrum [21]. Despite considerable advancements in the comprehension of gestational hypertension, numerous research deficiencies persist. It remains uncertain whether erythrocyte dysfunction is a key factor in the aetiology of hypertension or a secondary effect resulting from endothelial and placental pathology. Advanced methodologies, including proteomic and lipidomic analysis of erythrocyte membranes, may provide novel biomarkers and elucidate pathophysiological mechanisms [22,23]. Examining genetic variations in antioxidant enzymes like SOD2 and GPx1 may elucidate individual sensitivity. Additionally, novel treatment approaches aimed at alleviating erythrocyte oxidative stress such as nanoparticle antioxidants or erythrocyte-stabilizing agents present intriguing directions for future investigation.

Conclusion

Changes in red blood cells are an important but often overlooked part of gestational hypertension. Changes in the structure, biochemistry, and oxidation of red blood cells mess up microcirculation, make it harder for oxygen to get to the body, and make problems worse for both the mother and the baby. A lab test of erythrocyte function and oxidative balance can show how the disease affects the whole body and may help with early detection, risk assessment, and therapy monitoring. Integrating erythrocyte-focused biomarkers into clinical practice enables physicians and researchers to attain a comprehensive understanding of gestational hypertension, hence enhancing outcomes for both women and their infants.

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