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HEMATOLOGICAL AND COAGULATION CHANGES IN PHYSIOLOGICAL PREGNANCY

Abstract

The article presents a generalization of contemporary scientific data on hematological and coagulation changes during physiological pregnancy. It is shown that pregnancy is accompanied by significant adaptive alterations in the blood system, which ensure optimal conditions for fetal development, maintenance of placental circulation, and preparation of the maternal body for childbirth. The main components of these changes are highlighted, including hemodilution, physiological anemia of pregnancy, increased activity of the coagulation system, changes in platelet functional status, and features of fibrinolytic activity. It is noted that an increase in plasma volume by 40–50% leads to a relative decrease in hemoglobin and hematocrit levels, which is considered physiological anemia. The formation of a hypercoagulable state is described, обусловлене by increased levels of fibrinogen and coagulation factors (VII, VIII, X) and decreased activity of natural anticoagulants. It is emphasized that these changes are adaptive in nature; however, they are associated with an increased risk of thrombosis. The characteristics of the platelet component of hemostasis are analyzed, particularly the combination of a moderate decrease in platelet count with increased functional activity. It is shown that an imbalance between the coagulation and fibrinolytic systems may contribute to the development of

gestational complications. The important role of hormonal, endothelial, and immune mechanisms in the regulation of hemostasis during pregnancy and the necessity of considering them in clinical practice are emphasized.

Keywords: physiological pregnancy, fibrinolysis, gestational anemia, hypercoagulability, platelets, hemostasis.

Problem statement. Physiological pregnancy is accompanied by complex and multilevel changes in the blood system and hemostasis, which are adaptive in nature and aimed at ensuring normal fetal development, maintaining effective uteroplacental circulation, and preparing the woman's body for childbirth. One of the key features is the restructuring of hematological parameters and the formation of a state of relative hypercoagulability, which is necessary to prevent excessive blood loss during delivery [1].

At the same time, these physiological changes significantly complicate the clinical interpretation of laboratory parameters, since the boundary between normal and pathological conditions is rather conditional. In particular, conditions such as hemodilution, physiological anemia of pregnancy, or increased coagulation parameters may be misinterpreted as pathological or, conversely, may mask the development of complications. This creates difficulties for the timely diagnosis of disorders, including anemia, thrombophilic conditions, and thromboembolic complications.

Of particular importance is the problem of differentiating physiological adaptations from pathological changes, as an imbalance between the coagulation and fibrinolytic systems may lead to the development of severe gestational complications, including preeclampsia, placental insufficiency, and venous thromboembolism. In addition, the lack of clear pregnancy-specific reference values for certain laboratory parameters complicates the standardization of diagnostic approaches [7].

Thus, an in-depth study of hematological and coagulation changes during physiological pregnancy, as well as their clinical significance, is important for improving diagnostic efficiency, preventing complications, and optimizing the management of pregnant women.

Analysis of recent research and publications. Contemporary scientific studies indicate that physiological pregnancy is accompanied by complex changes in the hematological and coagulation systems, which are adaptive in nature and aimed at ensuring the normal course of gestation and childbirth [1–3]. The literature emphasizes that these changes result from the interaction of endocrine, vascular, and immune mechanisms.

Recent publications confirm that hemodilution and physiological anemia are normal components of pregnancy; however, they remain important subjects of differential diagnosis with pathological conditions [4–6]. Considerable attention is paid to iron deficiency as one of the most common complications affecting the course of pregnancy and perinatal outcomes [5].

In modern studies, pregnancy is considered a state of physiological hypercoagulability characterized by increased activity of coagulation factors and decreased fibrinolytic activity [7–9]. At the same time, an increased risk of thromboembolic complications is emphasized, especially in the presence of additional risk factors [9].

Particular attention is given to changes in the platelet component of hemostasis, including the combination of a moderate decrease in platelet count with increased functional activity [10–11]. The role of the endothelium, placenta, and immune mechanisms in the regulation of hemostasis and the development of gestational complications is also actively studied [16-18].

Despite the significant body of research, unresolved issues remain regarding the standardization of reference values for laboratory parameters during pregnancy and the improvement of approaches to the early diagnosis of hemostatic disorders.

Purpose of the article. To summarize current scientific data on hematological and coagulation changes during physiological pregnancy, their pathophysiological mechanisms, and clinical significance.

Presentation of the main material of the study. During pregnancy, plasma volume increases by approximately 40–50%, whereas erythrocyte mass increases to a lesser extent - by 20-30%, which leads to relative “dilution” of the blood [2].

Such changes are adaptive in nature, as decreased blood viscosity improves placental perfusion and enhances the transport of oxygen and nutrients to the fetus [3]. As a result, hemoglobin and hematocrit levels decrease, which clinically manifests as physiological anemia of pregnancy - a condition considered a variant of normal and reflecting maternal adaptation [4].

At the same time, in some pregnant women anemia becomes pathological, most often due to iron deficiency. Increased maternal demands associated with fetal and placental development, expansion of erythrocyte mass, and hormonal changes contribute to depletion of iron stores and the development of varying degrees of deficiency [5]. It has been established that iron deficiency may negatively affect intrauterine development, increase the risk of preterm birth and fetal growth restriction, and impair neuropsychological development of the fetus [6].

Therefore, timely diagnosis, particularly the assessment of ferritin levels, and early correction of iron deficiency in accordance with current clinical guidelines are of great importance [7]. It is also essential to perform differential diagnosis between physiological anemia and other forms, particularly megaloblastic anemia associated with folate or vitamin B12 deficiency, as management approaches and potential complications differ significantly [8].

Pregnancy is accompanied by the development of a physiological hypercoagulable state, which evolves gradually and reaches its maximum in the third trimester. Increased levels of fibrinogen, coagulation factors VII, VIII, and

X, as well as enhanced activity of von Willebrand factor, contribute to effective hemostatic protection during childbirth, when blood loss is physiologically inevitable [9]. At the same time, fibrinolytic activity decreases, particularly due to increased levels of plasminogen activator inhibitor (PAI-1), which leads to greater resistance of fibrin clots to lysis [10].

This balance between coagulation and fibrinolysis is adaptive, as it prevents excessive blood loss. However, it also creates conditions for increased thrombosis, explaining the more than fourfold rise in the risk of venous thromboembolism during pregnancy and the postpartum period [11]. In contemporary literature, pregnancy is considered a controlled but potentially high-risk hypercoagulable state, especially in the presence of additional factors such as obesity, thrombophilia, hypertension, or prolonged immobilization [12].

Hematological changes also involve the platelet component of hemostasis. In most pregnant women, a moderate decrease in platelet count is observed alongside increased functional activity. This condition, known as gestational thrombocytopenia, occurs in approximately 5–10% of cases and is usually mild and asymptomatic [13]. Platelet counts typically do not fall below 100×10^9/L and are not associated with pathological conditions such as immune thrombocytopenia or HELLP syndrome [14].

Increased platelet aggregability is associated with hormonal changes and enhanced expression of membrane glycoproteins, contributing to the formation of more stable thrombi [15]. This has important clinical implications, as the effectiveness of primary hemostasis during childbirth largely depends on the interaction between platelets and coagulation factors [16].

Additionally, pregnancy is associated with changes in the megakaryocytic lineage and platelet lifespan. Under the influence of estrogens and placental hormones, the proportion of younger, more functionally active platelets with

increased aggregative capacity rises [17]. These changes are adaptive and aimed at ensuring rapid hemostatic response to vascular injury during delivery [18].

At the same time, a marked decrease in platelet count or the appearance of atypical forms should be considered pathological findings requiring further evaluation, as they do not correspond to the physiological changes of pregnancy [19].

The hemostatic system during pregnancy functions in close interaction with the vascular endothelium, the placenta, and immune mechanisms. The placenta serves as an active source of tissue factor, which initiates the extrinsic coagulation pathway and forms a local hypercoagulable environment necessary for proper implantation and stable functioning of the placental complex [17]. At the same time, compensatory mechanisms are activated to limit excessive systemic coagulation, including increased levels of thrombomodulin and changes in protein C activity [18].

Disruption of this delicate balance underlies the development of gestational complications, primarily preeclampsia, which is characterized by endothelial dysfunction, reduced uteroplacental perfusion, and increased thrombogenesis [19]. According to current concepts, a key role in the pathogenesis of this condition is played by an imbalance between platelet activation, the coagulation system, and suppression of fibrinolysis [20].

The endothelium during pregnancy also undergoes functional remodeling, which significantly affects hemostatic balance. Under the influence of placental hormones, the synthesis of vasoactive substances, particularly nitric oxide and prostacyclin, increases, ensuring vasodilation and reducing platelet aggregation [20]. At the same time, the production of endothelin-1 and adhesion molecules increases, forming a complex regulatory system between anti-inflammatory and prothrombotic factors [21]. Disruption of this balance, especially under conditions of oxidative stress or placental dysfunction, may shift hemostasis toward

hypercoagulation and lead to complications ranging from preeclampsia to disseminated intravascular coagulation in severe cases [22].

Hemostatic changes are dynamic and depend on gestational age. In the first trimester, immune and endothelial adaptations predominate, whereas in the second and third trimesters, the most pronounced changes occur in the coagulation and fibrinolytic systems [23]. In late pregnancy, a significant increase in fibrinogen levels and activity of factors VII and VIII is observed, providing the so-called “hemostatic readiness” for delivery [24]. At the same time, structural modification of the fibrin clot occurs—it becomes denser and more resistant to fibrinolysis, which has a protective role in preventing excessive blood loss [25]. In combination with reduced fibrinolytic activity, this creates a specific hemostatic state unique to pregnancy.

Physiological changes in the coagulation system are also reflected in laboratory parameters, which may complicate their interpretation. For example, fibrinogen levels during pregnancy may reach 5–6 g/L, which outside pregnancy would be considered pathological but represents a normal variant during gestation [21]. D-dimer levels increase progressively throughout pregnancy and should not be interpreted as a sign of thrombosis in the absence of clinical symptoms. Similarly, activated partial thromboplastin time may be slightly shortened due to increased coagulation activity [22].

Therefore, for accurate assessment of hemostasis, it is necessary to use pregnancy-specific reference values, especially in patients at increased risk of thromboembolic complications [23].

The interaction between the coagulation and immune systems during pregnancy has become the subject of numerous recent studies. It has been established that proinflammatory cytokines, particularly interleukin-6 and tumor necrosis factor-α, can modulate the expression of tissue factor and influence thrombogenesis [24]. This partly explains the increased risk of thrombotic

complications in pregnant women with infections, gestational diabetes, or autoimmune diseases. Moreover, it has been shown that an imbalance between proinflammatory and anti-inflammatory mechanisms may alter the structure of fibrin and the stability of the clot, thereby affecting the course of pregnancy [25].

According to current concepts, hematological and coagulation changes during pregnancy should be considered as a complex integrated system of adaptations that includes hormonal, immune, vascular, and hemostatic mechanisms. The coordinated interaction of these processes ensures proper fetal development, maintenance of effective placental circulation, and readiness of the maternal body for physiological blood loss during childbirth [25]. At the same time, recent studies emphasize that even minor disturbances in this balance may lead to the development of clinically significant complications—from anemic conditions to thromboembolic events—which substantiates the need for careful monitoring of pregnant women throughout the entire gestational period.

Conclusions. Physiological pregnancy is accompanied by complex hematological and coagulation changes that are adaptive in nature and aimed at ensuring optimal conditions for fetal development, maintaining effective placental circulation, and preparing the maternal body for childbirth. The main components of these changes include hemodilution, physiological anemia, the formation of a hypercoagulable state, and functional remodeling of the platelet component of hemostasis.

It has been established that the balance between the coagulation and fibrinolytic systems is critically important for the normal course of pregnancy, while its disturbance may lead to the development of gestational complications, including preeclampsia, thromboembolic conditions, and placental insufficiency. Endothelial, hormonal, and immune mechanisms play a significant role in the regulation of hemostasis, and their interaction determines the stability of this balance.

Despite the physiological nature of most changes, they may complicate the clinical interpretation of laboratory parameters, which necessitates the use of pregnancy-specific reference values and an individualized approach to patient assessment. Thus, a deep understanding of the mechanisms of hematological and coagulation changes during pregnancy is essential for timely diagnosis of possible disorders, prevention of complications, and optimization of the management of pregnant women.

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