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EARLY GESTATIONAL BLEEDING AND SUBCHORIONIC HEMATOMA AS PREDICTORS OF FETAL GROWTH RESTRICTION: PATHOGENETIC MECHANISMS AND THE ROLE OF LOW-DOSE ASPIRIN

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Abstract. *Early gestational bleeding, including bleeding associated with subchorionic hematoma, is one of the most common complications of the first trimester of pregnancy and is increasingly regarded as a marker of impaired implantation and abnormal placentation. Growing evidence indicates that disturbances occurring during early placental development predispose to placental insufficiency, fetal growth restriction (FGR), and the delivery of infants with low birth weight. Subchorionic hematoma represents a localised manifestation of defective trophoblastic attachment and altered uteroplacental perfusion, and its presence has been associated with adverse perinatal outcomes, particularly in cases involving large hematoma volume or early gestational age at diagnosis.*

Low-dose acetylsalicylic acid (ASA) is widely used to prevent placental-mediated complications, including preeclampsia and FGR, due to its antiplatelet and vasodilatory effects. However, the use of ASA during early pregnancy remains controversial, as emerging data suggest a potential association with increased risk of subchorionic hematoma formation. This article reviews current evidence regarding the relationship between early pregnancy bleeding, subchorionic hematoma, placental insufficiency, and fetal growth restriction, with particular emphasis on the benefits and limitations of low-dose ASA in modifying perinatal risk and improving pregnancy outcomes.

Keywords: *early pregnancy bleeding, subchorionic hematoma, placental insufficiency, fetal growth restriction, low birth weight, low-dose aspirin.*

Introduction. Improvement of perinatal outcomes remains a major objective of modern obstetrics and perinatal medicine [1]. Over recent decades, clinical focus has shifted from the prevention of perinatal mortality alone toward optimisation of fetal development and reduction of long-term morbidity associated with adverse intrauterine conditions [2]. Among these conditions, fetal growth restriction occupies a central position due to its strong association with neonatal complications, neurodevelopmental impairment, and increased risk of chronic diseases in adulthood. Fetal growth restriction (FGR) remains one of the leading causes of perinatal morbidity and long-term adverse health outcomes [3]. Increasing evidence indicates that the origins of FGR lie in early gestation, during implantation and placental development [4].

Accumulating evidence suggests that the origins of FGR lie predominantly in early gestation, during the critical period of implantation and placental development [5]. Vaginal bleeding in the first trimester, observed in up to 25% of pregnancies, represents one of the earliest clinical manifestations of abnormal placentation [2,3]. Subchorionic hematoma, the most frequent ultrasound finding in women presenting with early pregnancy bleeding, has therefore attracted considerable attention as a potential marker of placental dysfunction and subsequent adverse perinatal outcomes [4–6].

At the same time, low-dose acetylsalicylic acid has become a cornerstone of preventive strategies targeting placental-mediated complications [7]. While its efficacy in reducing the incidence of preeclampsia and, in some populations, FGR is well established [8], uncertainty remains regarding the optimal timing of ASA initiation, particularly in women with early gestational bleeding or

subchorionic hematoma [9]. Low-dose acetylsalicylic acid (ASA) is widely used to prevent placental-mediated complications such as preeclampsia and FGR [10]. Understanding the complex interactions between early bleeding, placental development, FGR, and aspirin therapy is essential for improving individualised pregnancy management.

Vaginal bleeding during the first trimester is a frequent reason for obstetric consultation and is reported in approximately 15–25% of clinically recognised pregnancies [2,3]. The early gestational period encompasses implantation, trophoblast invasion, remodelling of spiral arteries, and establishment of the uteroplacental circulation [11]. Any disruption of these processes may have long-lasting consequences for placental structure and function.

Although spontaneous pregnancy loss remains the most immediate concern in women with early bleeding, increasing attention has been directed toward the long-term outcomes of ongoing pregnancies [2,8]. Numerous studies have demonstrated that first-trimester bleeding is associated with higher risks of preterm birth, placental abruption, low birth weight, and fetal growth restriction [2,3,8]. These associations persist even after exclusion of pregnancies ending in early miscarriage, supporting the concept that early bleeding reflects underlying placental pathology rather than an isolated event [8].

The aetiology of early gestational bleeding is multifactorial and includes chromosomal abnormalities, endocrine disorders, immunological mechanisms, infectious and inflammatory conditions, and extragenital maternal pathology [1,9]. However, in a substantial proportion of cases, no definitive cause can be identified, further complicating risk stratification and clinical decision-making [2,3].

Subchorionic hematoma is defined as an accumulation of blood between the chorionic membrane and the uterine wall resulting from partial detachment of the trophoblast from the endometrium [4]. Sonographically, SCH appears as a hypoechoic or anechoic area adjacent to the gestational sac, occasionally containing echogenic components corresponding to clotted blood [7].

Reported prevalence of SCH varies widely, ranging from less than 1% in asymptomatic pregnant women to approximately 20% among those presenting with threatened miscarriage [4–6]. This variability reflects differences in study populations, ultrasound resolution, gestational age at examination, and diagnostic criteria [5,6].

Ultrasonography remains the gold standard for SCH diagnosis and follow-up [4,7]. Advances in imaging technology have substantially improved detection rates, suggesting that earlier reports may have underestimated true prevalence [7]. Serial ultrasound examinations are often used to monitor hematoma size, location, and resolution, as these parameters may influence pregnancy prognosis [6,10].

The clinical significance of SCH remains a subject of ongoing debate [5,6,10]. Numerous studies have demonstrated associations between SCH and adverse pregnancy outcomes, including spontaneous miscarriage, placental abruption, preterm birth, and fetal growth impairment [5,6,8,10]. Meta-analyses consistently confirm an increased risk of early pregnancy loss in women with SCH, particularly when hematomas are large or diagnosed at earlier gestational ages [5,10].

The relationship between SCH and fetal growth restriction is of particular interest. Several investigators have reported lower birth weights, increased rates of FGR, and higher neonatal intensive care unit admission rates among infants born after pregnancies complicated by SCH [5,6,10]. These findings support the hypothesis that SCH represents a marker of impaired placentation and persistent uteroplacental dysfunction [9,10].

Hematoma size appears to be one of the most important prognostic factors. Large hematomas occupying a substantial proportion of the gestational sac have been associated with significantly poorer outcomes compared to smaller lesions [6,12]. Gestational age at diagnosis also plays a role, with earlier detection generally indicating a higher risk of adverse outcomes [6,10].

Placental insufficiency is widely regarded as the principal mechanism linking early gestational bleeding and SCH with fetal growth restriction [9,11–13]. Abnormal trophoblast invasion and inadequate remodelling of spiral arteries result in reduced uteroplacental blood flow, chronic fetal hypoxia, and impaired nutrient transfer [9,12].

In pregnancies complicated by SCH, local bleeding and hematoma formation may further exacerbate placental hypoperfusion by increasing oxidative stress, inflammation, and mechanical disruption at the maternal–fetal interface [9,10,14]. Elevated levels of pro-inflammatory cytokines, such as interleukin-1, interleukin-8, and tumour necrosis factor, have been implicated in disturbances of uteroplacental hemostasis and immune tolerance, contributing to placental dysfunction [12].

FGR accounts for nearly one-third of all low birth weight neonates and is associated with increased perinatal morbidity and long-term health consequences, including cardiovascular and metabolic disease in adulthood [15,16]. Ultrasound-based fetal biometry remains the diagnostic gold standard, as clinical assessment alone detects only a minority of affected pregnancies [17].

Fetal growth restriction is therefore increasingly viewed as a clinical manifestation of placental insufficiency rather than an isolated fetal condition [11,13]. This paradigm shift has important implications for early risk assessment and preventive strategies.

According to World Health Organisation data, the prevalence of FGR varies widely across regions, exceeding 30% in some low-resource settings and remaining below 7% in developed European countries [15]. In the United States, FGR is diagnosed in approximately 10–15% of births, while reported rates in the Russian Federation range from 2.4% to 17% [11,13].

Infants with FGR account for nearly one-third of all low birth weight neonates and are at increased risk of perinatal morbidity, including respiratory distress, hypoglycemia, hypothermia, and intrapartum hypoxia [11,13]. Long-term consequences include impaired neurodevelopment, increased susceptibility to cardiovascular and metabolic diseases, and reduced life expectancy [16].

Accurate diagnosis of FGR relies on precise determination of gestational age and ultrasound-based fetal biometry [11,13,14]. Clinical assessment alone identifies only a minority of affected pregnancies, underscoring the importance of early and repeated ultrasound evaluation in high-risk populations [14].

Acetylsalicylic acid exerts its primary effect through irreversible inhibition of platelet cyclooxygenase, leading to reduced thromboxane A_2 synthesis and decreased platelet aggregation [18]. These effects improve microcirculatory blood flow and provide a physiological basis for ASA use in preventing placental-mediated complications [19]. At low doses, ASA selectively inhibits thromboxane production while preserving prostacyclin activity, resulting in vasodilation and improved microcirculatory perfusion [20].

In the context of pregnancy, low-dose ASA has been shown to enhance uteroplacental blood flow, promote spiral artery remodelling, and reduce the formation of microthrombi in the placental circulation [17–19]. These effects provide a strong physiological rationale for its use in preventing placental-mediated complications, including preeclampsia and FGR [17–20]. Meta-analyses demonstrate that ASA initiated before 16 weeks of gestation significantly reduces the incidence of preeclampsia and, in selected high-risk populations, fetal growth restriction and preterm birth [21].

Multiple randomised controlled trials and meta-analyses have demonstrated that initiation of low-dose ASA before 16 weeks of gestation reduces the incidence of preeclampsia, particularly its early-onset form [17–19]. Importantly, several studies have also reported a reduction in the risk of FGR and preterm birth, especially in women at high risk of placental insufficiency [22].

Current clinical guidelines recommend low-dose ASA for women with established risk factors for placental-mediated complications, including a history of preeclampsia or FGR, chronic hypertension, diabetes mellitus, autoimmune disorders, renal disease, and multifetal gestation [23]. These recommendations reflect the growing recognition of ASA as a key component of preventive obstetric care.

Despite its benefits, the use of ASA during the first trimester remains controversial. Emerging evidence suggests that ASA may increase the likelihood of subchorionic hematoma formation, particularly when initiated early in gestation [24]. This association raises concerns regarding the balance between potential benefits in improving placental perfusion and the risk of exacerbating bleeding-related complications.

Several observational studies have reported higher rates of SCH in women receiving antiplatelet or anticoagulant therapy during early pregnancy [22,24]. While causality has not been definitively established, these findings suggest that careful consideration of timing, dosage, and individual risk factors is essential.

Some authors advocate postponing ASA initiation until the second trimester in women presenting with active vaginal bleeding or SCH, particularly when hematomas are large or persistent [25]. However, robust prospective data addressing this issue are currently lacking. Although a direct causal relationship has not been definitively established, these findings raise concerns regarding ASA initiation in women with active vaginal bleeding or large SCH.

Women with early gestational bleeding or SCH should be considered at increased risk of placental insufficiency and FGR [5,6,10]. Serial ultrasound monitoring of placental structure, uteroplacental blood flow, and fetal growth is recommended in these pregnancies. Doppler assessment of uterine and umbilical arteries may provide additional prognostic information [14]. SCH should therefore be regarded as a localised manifestation of abnormal placentation rather than an isolated ultrasound finding.

The decision to initiate or continue low-dose ASA should be individualised, taking into account the severity of bleeding, hematoma characteristics, and the presence of established risk factors for placental-mediated complications [17–21,24]. Multidisciplinary management involving obstetricians, maternal–fetal medicine specialists, and, when necessary, haematologists may optimise outcomes in high-risk cases.

First-trimester vaginal bleeding has been consistently associated with an increased risk of adverse pregnancy outcomes, including spontaneous miscarriage, preterm birth, placental abruption, and low birth weight [2,3,8]. Population-based studies demonstrate that even when pregnancy continues beyond the first trimester, early bleeding is associated with reduced gestational age at delivery and impaired fetal growth [2,8].

Conclusion. Early gestational bleeding, particularly when associated with subchorionic hematoma, represents an important clinical marker of abnormal placentation and increased risk of fetal growth restriction. Placental insufficiency serves as the central pathogenetic link between early pregnancy complications and adverse perinatal outcomes.

Low-dose aspirin offers a promising strategy for improving uteroplacental perfusion and reducing the risk of FGR; however, its use in early pregnancy requires careful risk–benefit assessment due to a potential association with bleeding-related complications. Personalised management, early identification of high-risk pregnancies, and further prospective research are essential for optimising the use of aspirin and improving perinatal outcomes. Early identification of high-risk pregnancies and tailored preventive strategies are essential for improving perinatal outcomes.

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