EPIDEMIOLOGICAL ASPECTS AND CLINICAL IMPORTANCE OF PLACENTAL INSUFFICIENCY AND FETAL GROWTH RESTRICTION (LITERATURE REVIEW)

Nargiza B. Iminova - assistant
Khayitkhon B. Abdurashidova - assistant
Andijan State Medical Institute (Tashkent, Uzbekistan)

Abstract. *Placental insufficiency (PI) remains one of the most critical complications of pregnancy, with profound implications for maternal and perinatal health. Despite global progress in maternal care, the incidence of PI has remained largely unchanged over the past decades. According to clinical observations, PI is detected in approximately 22-35% of pregnancies, while in high-risk groups-such as women with preeclampsia, chronic somatic disorders, intrauterine infections, or uterine malformations-the incidence increases to 45-77%.*

Key words: *placental insufficiency, fetal growth restriction, perinatal health.*

Introduction. Placental insufficiency remains one of the most critical complications of pregnancy, with profound implications for maternal and perinatal health. Despite global progress in maternal care, the incidence of PI has remained largely unchanged over the past decades [3,6,9]. According to clinical observations, PI is detected in approximately 22-35% of pregnancies, while in high-risk groups-such as women with preeclampsia, chronic somatic disorders, intrauterine infections, or uterine malformations-the incidence increases to 45-77%. The impact of PI on perinatal morbidity and mortality is substantial. It is identified in 34-41% of cases of perinatal mortality, and when combined with other complications of pregnancy, PI contributes to as many as two-thirds of adverse outcomes. In 24-45% of affected pregnancies, PI leads to fetal growth restriction (FGR), a condition strongly associated with hypoxia, intrauterine distress, and long-term developmental disorders [1,5,7]. The persistence of such high rates highlights the need for a deeper understanding of PI and FGR as interrelated conditions within the functional system “mother-placenta-fetus.” From both theoretical and clinical perspectives, they are considered maladaptive processes that disrupt the delicate balance of maternal and fetal physiology [2,7,8]. Placental insufficiency is defined as a pathological condition in which the placenta fails to provide adequate gas exchange, nutrient transfer, and endocrine function to meet the demands of the growing fetus. Two principal forms are distinguished: 1. Primary PI, which develops before 16 weeks of gestation. This form is usually the result of defective implantation or abnormal placentation, leading to impaired trophoblast invasion and inadequate remodeling of the uterine spiral arteries.

Secondary PI, which develops after 16 weeks of gestation, often as a consequence of maternal systemic disease, infectious processes, or complications arising during pregnancy. By clinical presentation, PI may be: Acute, with a sudden onset, frequently associated with placental abruption or vascular catastrophe. This form is relatively rare but carries a high risk of intrauterine fetal demise. Chronic, characterized by a progressive course with gradually worsening placental function. Chronic PI is the predominant form and is closely associated with FGR and chronic hypoxia. Pathogenetically, PI can be further divided into: Hemodynamic type, caused by impaired uteroplacental or fetoplacental circulation. Placental-membrane type, associated with disturbances in transplacental transport of oxygen, nutrients, and metabolic products. Cellular-parenchymal type, involving structural and functional damage of the villous tissue, frequently associated with degenerative or inflammatory changes. This classification has both diagnostic and prognostic value, as it provides a framework for understanding the diverse mechanisms leading to PI. The development of PI is multifactorial. The central event is inadequate invasion of the cytotrophoblast into the uterine wall and insufficient remodeling of spiral arteries [3,9,13]. Normally, spiral arteries transform from narrow, high-resistance vessels into low-resistance channels capable of providing continuous blood flow to the intervillous

space. In PI, this process is incomplete, leading to persistent vasospasm, episodic ischemia, and ultimately hypoperfusion of the placenta. At the cellular level, hypoxia induces endothelial dysfunction, alters the balance of vasoactive mediators (such as nitric oxide and endothelin), and promotes oxidative stress. Excess production of reactive oxygen species damages cell membranes, proteins, and DNA, further compromising placental function [2,3,5]. Apoptotic activity in the villous trophoblast is markedly increased in PI, contributing to the thinning of the syncytiotrophoblast layer and reduced efficiency of exchange processes. At the same time, inflammatory cytokines and angiogenic imbalance (VEGF/PlGF deficiency, sFlt-1 overexpression) play a significant role in disrupting placental angiogenesis [2,4,16]. Thus, PI represents a complex pathological process that integrates hemodynamic, molecular, and structural abnormalities, culminating in inadequate support for fetal growth and development. Fetal growth restriction (FGR) is one of the most clinically significant consequences of PI. It is defined as a condition in which the fetus fails to achieve its genetically predetermined growth potential due to adverse intrauterine conditions [8,14]. Two main forms are recognized: Symmetric FGR, usually associated with early disturbances such as genetic abnormalities, chromosomal disorders, or intrauterine infections. In this type, all biometric parameters (head, abdomen, femur length) are proportionally reduced. Asymmetric FGR, typically developing in the second or third trimester as a result of PI. This form is characterized by relative preservation of head growth, with pronounced lag in abdominal circumference, reflecting impaired hepatic and subcutaneous fat deposition. A key diagnostic challenge is differentiating FGR from small-for-gestational-age (SGA) fetuses. SGA fetuses are constitutionally small but otherwise healthy, whereas true FGR is pathologic and associated with a high risk of hypoxia, metabolic acidosis, intrauterine distress, and perinatal mortality [3,4,6,8,11]. Long-term outcomes of FGR are equally concerning. Children born with intrauterine growth restriction are predisposed to neurodevelopmental delay, impaired cognitive performance, and metabolic disorders in later life, including obesity, insulin resistance, and cardiovascular disease. The etiology of PI and FGR is multifactorial, with contributions from maternal, fetal, and environmental factors [14,16]. Socioeconomic and lifestyle factors: poor nutrition, smoking, alcohol or drug use, and chronic stress. Maternal somatic diseases: hypertension, preeclampsia, diabetes mellitus, chronic kidney disease, and cardiovascular pathology. Gynecological and obstetric factors: congenital uterine anomalies, endometrial scarring, recurrent pregnancy loss, and intrauterine infections [12,13]. Complications of current pregnancy: gestosis, Rh-isoimmunization, oligohydramnios, and multiple pregnancy. Genetic and chromosomal abnormalities: including trisomies, microdeletions, and syndromic conditions associated with impaired growth potential. Understanding these risk factors allows for the identification of high-risk pregnancies and the implementation of early monitoring and preventive strategies [7,9]. The diagnosis of PI and FGR relies on a combination of clinical, instrumental, and laboratory methods [5,8]. Ultrasound biometry remains the gold standard for assessing fetal growth. Serial measurements of biparietal diameter, abdominal circumference, and femur length provide valuable information on growth dynamics. Doppler velocimetry of the uterine, umbilical, and middle cerebral arteries is crucial for evaluating hemodynamic changes [1,18]. Abnormalities such as absent or reversed end-diastolic flow in the umbilical artery are strong predictors of adverse perinatal outcome. Cardiotocography provides functional assessment of the fetus, allowing detection of hypoxia and compromised adaptation. Biochemical and hormonal markers, including placental proteins, human chorionic gonadotropin, progesterone, and estriol, can complement instrumental methods by reflecting the secretory and metabolic capacity of the placenta [4,9]. Early and accurate diagnosis is vital, as it guides the timing of delivery, selection of therapeutic interventions, and monitoring strategies [3,7,12]. Modern concepts emphasize that the placenta is not an isolated organ, but a central component of the dynamic functional system “mother-placenta-fetus.” Placental insufficiency should therefore be regarded as a maladaptive process within this system rather than a discrete disorder [6,8,11]. Recognition of PI as a systemic dysfunction highlights the importance of

integrative approaches in both diagnosis and management. Preventive strategies should target maternal health optimization before and during pregnancy, while therapeutic measures should focus on improving uteroplacental perfusion and fetal adaptation [12,18]. Despite advances in perinatal medicine, the burden of PI and FGR remains high, necessitating continued research into their molecular mechanisms, early diagnostic markers, and effective therapeutic interventions.

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