



# EVALUATION OF UTERINE MICROCIRCULATION AS A KEY FACTOR IN THE PATHOGENESIS OF REPRODUCTIVE LOSS

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<b>Article history:</b>	<b>Abstract:</b>
<p><b>Received:</b> 24<sup>th</sup> August 2025 <b>Accepted:</b> 20<sup>th</sup> September 2025</p>	<p><b>Relevance:</b> Reproductive losses remain one of the most complex and multidisciplinary problems in modern obstetrics. Despite numerous established etiological factors, a key pathogenetic link is often the disruption of utero-placental blood flow, which is based on disorders at the microcirculatory level. Early diagnosis of these conditions is crucial for preventing pregnancy loss.</p> <p><b>Objective:</b> To systematize and analyze current scientific data on the role of microcirculatory disorders in the genesis of reproductive losses, as well as to review and evaluate modern diagnostic methods with an emphasis on non-invasive technologies.</p> <p><b>Materials and Methods:</b> An analysis and synthesis of data from domestic and foreign scientific publications on microcirculatory disorders in the "mother-placenta-fetus" system were conducted. Special attention was given to the methodology and clinical potential of Laser Doppler Flowmetry (LDF) as a tool for early preclinical diagnosis.</p> <p><b>Results:</b> The review demonstrated that reproductive losses are often based on endothelial dysfunction, leading to a spastic type of microcirculatory disturbance in the endometrium and the developing placenta. This causes local ischemia, oxidative stress, and consequently, placental insufficiency. Methods like LDF allow for the quantitative assessment of tissue perfusion and the detection of pathological changes at a stage when standard methods (e.g., uterine artery dopplerometry) are not yet informative.</p> <p><b>Conclusions:</b> The assessment of microcirculation is a promising area for the diagnosis and prediction of reproductive losses. The implementation of highly sensitive methods such as LDF into clinical practice opens up opportunities for the early identification of high-risk groups and the development of personalized therapeutic and prophylactic interventions.</p>

**Keywords:** Reproductive loss, miscarriage, microcirculation, endothelial dysfunction, utero-placental blood flow, placental insufficiency, laser doppler flowmetry (LDF).

## INTRODUCTION

The problem of reproductive loss, including recurrent miscarriage, antenatal fetal death, and severe forms of placental insufficiency, remains an ongoing concern in modern obstetrics and gynecology. This pathology is multifactorial, encompassing genetic, endocrine, infectious, inflammatory, and immunological causes. However, despite the diversity of triggers, the final common link in the pathogenesis in most cases is disturbances in the uteroplacental circulation. Central to these disturbances are disturbances at the level of microcirculation—the final and most important part of the vascular system, where transcapillary exchange processes occur.

The microcirculatory bed, consisting of arterioles, capillaries, venules, and arteriovenous anastomoses, is a functional unit responsible for the delivery of oxygen

and nutrients to tissues and the removal of metabolic waste products. Adequate endometrial perfusion is essential for successful blastocyst implantation, subsequent trophoblast invasion, and the formation of a healthy placenta. Any disruption to this finely tuned mechanism early in gestation can lead to placentation defects and, consequently, to the development of placental insufficiency, fetal growth restriction, and miscarriage.

Traditional methods for assessing uterine blood flow, such as uterine artery Doppler ultrasound, allow for the diagnosis of hemodynamic disturbances primarily at the macroscopic level and, as a rule, after clinical manifestations have already been established. Therefore, there is an urgent need to identify and implement methods capable of detecting microcirculatory disorders at the preclinical stage,



allowing for timely preventive and therapeutic interventions. The purpose of this review is to systematize concepts regarding the role of microcirculatory disorders in the pathogenesis of reproductive losses, based on an analysis of current scientific literature, and to evaluate the diagnostic capabilities of modern noninvasive diagnostic methods, particularly laser Doppler flowmetry.

### **Pathogenetic Aspects of Microcirculatory Disorders in Reproductive Loss**

The endothelium plays a fundamental role in regulating vascular tone and maintaining homeostasis within the microcirculatory bed. Endothelial dysfunction is a universal pathophysiological mechanism underlying many obstetric complications. Under the influence of various damaging factors (toxic, hypoxic, immune), the balance between the production of vasodilators (nitric oxide, prostacyclin) and vasoconstrictors (endothelin-1, thromboxane A<sub>2</sub>) is disrupted. The predominance of vasoconstrictor stimuli leads to generalized arteriolar spasm, a key characteristic of spastic microcirculatory disorders. This spasm leads to decreased tissue perfusion, developing ischemia and hypoxia in the endometrium and chorionic villi. Chronic hypoxia, in turn, triggers a cascade of pathological reactions, including oxidative stress, activation of lipid peroxidation, and damage to cell membranes. As a result, cytotrophoblast invasion of the spiral arteries is impaired, which is the morphological basis for the development of placental insufficiency. Thus, a vicious cycle is established, in which initial microcirculation disturbances lead to structural and functional placental defects, which, in turn, exacerbate hypoxia and ischemia.

### **Modern Methods for Diagnosing Microcirculation Disorders**

Assessing microcirculation is a complex task requiring the use of highly sensitive technologies. In recent years, laser Doppler flowmetry (LDF) has become widely used for this purpose in various fields of medicine. This method is based on recording changes in the frequency of laser radiation reflected from moving red blood cells in the tissue volume being studied. LDF allows for real-time, noninvasive quantitative data on tissue perfusion (microcirculation).

The key advantages of LDF are its objectivity, high sensitivity to the slightest changes in blood flow, and the ability to conduct long-term monitoring. The method allows for assessing the basal perfusion level (parameter M), its variability ( $\sigma$ ), and the coefficient of variation (Kv). A combined analysis of these parameters provides a comprehensive understanding of the state of microcirculation:

· Parameter M (microcirculation) reflects the average level of blood flow in the tissue. A decrease in this parameter indicates ischemia.

· Parameter  $\sigma$  (standard deviation) characterizes the temporal variability of perfusion, reflecting the modulating influence of active (myogenic, neurogenic) and passive (respiratory, cardiac) mechanisms controlling vascular tone. · The coefficient of variation (Kv), calculated as the ratio of  $\sigma$  to M, is an integral indicator reflecting the state of microcirculation. An increase in this An increase in this indicator indicates an improvement, while a decrease indicates a deterioration in microcirculation.

The use of LDF in obstetric practice allows for the diagnosis of various types of microcirculation disorders early in pregnancy, in particular, the identification of the spastic hemodynamic type, which is a predictor of placental insufficiency and other pregnancy complications.

### **DISCUSSION**

Analysis of the literature suggests that microcirculation disorders are not simply a consequence, but rather one of the triggers in the pathogenesis of reproductive losses. Endothelial dysfunction and subsequent microvascular spasm lead to a cascade of events culminating in inadequate placentation and the development of chronic placental insufficiency.

The introduction of methods such as LDF into clinical practice is changing the paradigm for the care of patients with reproductive losses. Instead of identifying already developed complications using traditional methods (ultrasound, Doppler ultrasound), it is now possible to identify pathological changes at a preclinical, functional level. This allows for the identification of high-risk groups during the planning stage or in the earliest stages of pregnancy.

Early detection of spastic microcirculation in women with a complicated obstetric history can serve as the basis for preemptive pathogenetic therapy aimed at correcting endothelial dysfunction, improving blood rheology, and normalizing vascular tone. Subsequent LDF monitoring allows for an objective assessment of the effectiveness of treatment and preventive measures and, if necessary, promptly adjusting management strategies.

### **CONCLUSION**

Microcirculatory disturbances in the maternal-placental-fetal system play a key role in the pathogenesis of reproductive losses. Understanding these mechanisms and the use of modern diagnostic tools open new prospects for the prevention of obstetric complications. Laser Doppler flowmetry is a highly informative, non-invasive, and objective method for detecting



microcirculatory disorders at the preclinical stage. Its use can significantly improve the quality of diagnostics and facilitate the development of personalized approaches to the care of patients with a high risk of reproductive loss, thereby improving perinatal outcomes. Further research in this area is necessary to standardize the technique and determine its precise role in the algorithms for examining pregnant women.

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