Fetal growth restriction (FGR) is a pregnancy complication that consists in the inability of the fetus to achieve its genetically predicted growth potential. It affects about 5 to 10% of pregnancies and is the second most common cause of perinatal mortality. The aim of the research is to assess the influence of placental hypoxia and oxidative stress damage for alterations in endothelial adherens junctions (AJs) in pregnancy complicated with FGR. Moreover, the aim of the project is to evaluate if the disrupted placento-maternal exchange can lead to desintegration of fetal blood-brain barrier (BBB) and result in appearance of adherens junctions proteins (AJPs) and neuronal damage factors in umbilical blood. Furthermore, the objective is to assess the relationship between the neurovascular unit damage and the early neonatal outcomes, such as inapproproate neurological pattern (hypotonia, hypertonia, dystonia, hyperxcitability), intraventricular haemorrhage (IVH) and periventricular leucomalacia (PVL). Finally, the possibility of prediction the above mentioned adverse perinatal outcomes, before comfirmation them in neuroimaging, on the basis of examined endothelial and neuronal parameters will be checked.

FGR increases an infants' lifelong risk of adverse health outcomes including long-term poor neurological development, poor postnatal growth, and other childhood conditions, such as serious and long-lasting immune deficiencies. Even well beyond infancy and childhood, FGR is associated with a significant increase in the risk of cardiovascular disease, diabetes mellitus and hyperinsulinemia. Prenatal diagnosis of growth-restricted fetuses is clinically important due to the high risk of morbidity and mortality in this group. Moreover, it is important to determine the optimal time of pregnancy termination and to prevent obstetric complications. Low birth weight has its long-term consequences, which results from the intrauterine programming of the nervous system. Considering that fetal growth restriction is a complication of 5-10% of pregnancies, associated with a high percentage of intrauterine deaths, reaching 19,8% in cases not diagnosed prenatally, the search for non-invasive markers, to predict the condition of the newborn and to use them in the future monitoring of pregnancy, is justified from a social point of view.

The project involves analysis of utero-placental circulatory disorders in pregnancies complicated with FGR in relation to expression of placental AJPs (VE-cadherin, P-cadherin, integrin α6β4, α-catenin, β-catenin, PECAM-1), hypoxia markers (HIF1α, BNIP3, PDK1, GLUT1, VEGF) and oxidative stress factors (8-OHdG, LPO, MDA, apurinic/apyrimidinic sites). Moreover, the endothelial and neuronal damage and changes in the BBB permeability will be checked in pregnancies complicated with FGR, assessing by the concentration of selected AJPs (ICAM-1, VCAM-1, selectin E, VE-cadherin, integrin α6β4, α-catenin, β-catenin) and neuronal damage proteins (NR2, caspase-3, AM, activin A, G-FAP, BDNF) in umbilical blood.

Circulatory disorders associated with FGR may destroy the endothelial connections and lead to the appearance of endothelial damage markers in umbilical blood. In addition, placental insufficiency and the associated vascular pathology may be associated with altered expression of AJPs. Endothelial damage may contribute to an increase in the permeability of the blood-brain barrier, which is the anatomical and biochemical barrier between blood vessels and the nervous system. Its destruction and increased permeability may be evidenced by the appearance of markers of neuronal damage in umbilical blood.

The planned research is an attempt to analyze the influence of maternal-fetal exchange disturbances on changes in the expression of AJPs in placental tissues in response to prenatal hypoxia and oxidative stress. The research will allow to determine whether the disorders of placental function in a pregnancy complicated with FGR are reflected in markers appearing in umbilical blood. Thanks to this, it would be possible to select specific markers that would provide information on endothelial function, the permeability of the blood-brain barrier and the state of nerve cells. The search for such substances would make it possible to precisely monitor fetuses with FGR and to optimize the time of pregnancy termination to prevent intrauterine damage of the central nervous system and enable the prognosis of the newborn condition after delivery, especially neurological complications before positive neuroimaging tests.