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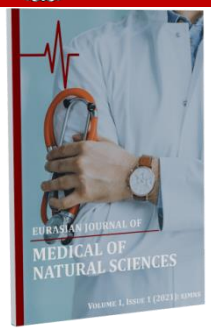

THE SIGNIFICANCE OF ELEVATED HOMOCYSTEINE LEVELS IN FETAL DEVELOPMENT DISRUPTION

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ABSTRACT

Elevated serum homocysteine levels (hyperhomocysteinemia) represent a significant risk factor for fetal developmental disorders during pregnancy. High concentrations of homocysteine exert a toxic effect on the vascular endothelium, lead to impaired placental circulation, increase the risk of thrombophilic complications, and can cause neural tube defects, intrauterine growth restriction, preeclampsia, and even pregnancy loss. This article discusses the pathogenetic mechanisms of hyperhomocysteinemia's effect on embryogenesis, the clinical consequences for the fetus, and current methods for diagnosing and correcting this condition, including the use of folic acid, B vitamins, and anticoagulant therapy, with an emphasis on data from the last five years.

Introduction: Intrauterine fetal development disorders, such as fetal growth restriction (FGR), represent a serious problem in obstetrics, holding a leading position in the structure of perinatal morbidity and mortality. According to various sources, the incidence of FGR ranges from 5% to 10%. In recent years, there has been growing evidence of a potential link between elevated serum homocysteine levels and adverse pregnancy outcomes, as well as subfertility. Homocysteine, a sulfur-containing amino acid, plays an important role in various biochemical processes. Its elevated levels are a recognized risk factor for cardiovascular diseases, neurodegenerative disorders, and other health problems. However, its association with subfertility and embryonic development disorders remains an area of active research. Understanding this connection opens new perspectives for diagnosis and prevention, allowing for the identification of risk groups and the development of targeted interventions. Folic acid and B vitamins, particularly B12 and B6, play a key role in homocysteine metabolism. Deficiencies in these nutrients can lead to homocysteine accumulation.

Methods. This review is based on an analysis of scientific publications from the last five years on the impact of hyperhomocysteinemia on fetal development and reproductive health. In this study, patients provided informed consent, and the protocol was approved by a local ethics committee. Inclusion criteria for the original study included age from 19 to 40 years, singleton pregnancy, normal fetal anatomy, and a BMI of 21 to 30 kg/m2, with no preeclampsia. Patients with multiple pregnancies, fetal chromosomal abnormalities, a history

of FGR, diabetes, hematological and autoimmune diseases, and other confounding factors were excluded.

Results. Analysis of contemporary literature and the results of the aforementioned prospective study confirm the negative impact of hyperhomocysteinemia on the course of pregnancy and fetal development. The study revealed that patients with fetal growth restriction (FGR) had significantly higher median homocysteine concentrations at 10-16 weeks (19.65 mmol/L), 22-24 weeks (18.49 mmol/L), and 30-32 weeks (15.36 mmol/L) compared to the control group ($p<0.05$). Notably, homocysteine concentration remained stably high throughout pregnancy in the FGR group, whereas a decrease was observed in the control group. ROC analysis determined optimal threshold levels of homocysteine concentration for predicting risks at different stages of pregnancy. For example, for the 10-14 week period, the threshold level was 14.9 mmol/L. Data from the last five years also indicate a link between elevated homocysteine and an increased risk of preeclampsia, placental abruption, neural tube defects, and low birth weight.

Conclusion. Elevated serum homocysteine is a significant risk factor associated with various pregnancy complications and fetal development disorders, as well as fertility problems. Research findings from the last five years confirm the importance of monitoring homocysteine levels in women during preconception and pregnancy. The proposed threshold level for intervention is 13.5 mmol/L. The prevalence of hyperhomocysteinemia may indicate a deficiency of micronutrients such as vitamins B6, B12, and folic acid. Timely correction of these deficiencies and normalization of homocysteine levels can contribute to improved reproductive outcomes. Nevertheless, further large-scale studies are needed to fully establish the role of hyperhomocysteinemia in unexplained infertility and to develop optimal prevention and treatment strategies.

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