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PREDICTION OF PREECLAMPSIA DEVELOPMENT IN PREGNANT WOMEN AFTER IN VITRO FERTILIZATION

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Abstract

Preeclampsia remains one of the most common and clinically significant complications of pregnancy, particularly in women who conceive using assisted reproductive technologies, including in vitro fertilization (IVF). Impaired implantation, endothelial dysfunction, immune-inflammatory activation and hemostatic disturbances are considered key pathogenic mechanisms contributing to the development of this condition, which determines the need for early predictive markers.

Aim. To evaluate the predictive value of clinical, laboratory and Doppler parameters for the development of preeclampsia in pregnant women after IVF.

Materials and Methods. A prospective study included 80 pregnant women after IVF and 40 women with spontaneous pregnancies. At 11–14 weeks of gestation, serum levels of lactate dehydrogenase (LDH), homocysteine, C-reactive protein (CRP), D-dimer and vitamin D were measured. Coagulation parameters and Doppler indices of the uterine arteries (PI, RI, S/D) were also assessed. Statistical analysis included chi-square testing, odds ratio (OR) calculation, logistic regression and evaluation of predictive models.

Results. The incidence of preeclampsia in the IVF group was 30%. Women who subsequently developed preeclampsia demonstrated significantly higher levels of LDH, homocysteine, CRP and D-dimer, as well as vitamin D deficiency ($p<0.05$). According to univariate analysis, LDH (OR=3.8), homocysteine (OR=3.5) and CRP (OR=2.4) showed the highest predictive value. Multivariate analysis identified elevated LDH and hyperhomocysteinemia as independent predictors. Increased uterine artery resistance on Doppler examination further improved predictive accuracy.

Conclusion. Combined assessment of biochemical markers and Doppler parameters enables early identification of high-risk patients after IVF and supports individualized prevention strategies for preeclampsia.

Keywords: in vitro fertilization, preeclampsia, prediction, biomarkers, hemostasis, Doppler ultrasound.

ПРОГНОЗИРОВАНИЕ РАЗВИТИЯ ПРЕЭКЛАМПСИИ У БЕРЕМЕННЫХ ПОСЛЕ ЭКСТРАКОРПОРАЛЬНОГО ОПЛОДОТВОРЕНИЯ

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Аннотация.

Преэклампсия является одним из наиболее частых и клинически значимых осложнений беременности, особенно у пациенток, беременность которых наступила в результате экстракорпорального оплодотворения (ЭКО). Нарушения имплантации, дисфункция эндотелия, иммуновоспалительная активация и изменения системы гемостаза рассматриваются как ключевые

патогенетические механизмы формирования данного осложнения, что обуславливает необходимость поиска ранних прогностических маркеров.

Цель исследования — оценить прогностическую значимость клинико-лабораторных и допплерометрических показателей в развитии преэклампсии у беременных после ЭКО.

Материалы и методы. В проспективное исследование включены 80 беременных после ЭКО и 40 женщин со спонтанной беременностью. В 11–14 недель гестации определяли уровни лактатдегидрогеназы (ЛДГ), гомоцистеина, С-реактивного белка (СРБ), D-димера, витамина D, показатели коагулограммы, а также допплерометрические параметры маточных артерий (PI, RI, S/D). Статистический анализ включал расчет χ^2, отношения шансов (OR), логистическую регрессию и оценку прогностической модели.

Результаты. Частота преэклампсии в группе ЭКО составила 30%. У пациенток с развившейся преэклампсией достоверно чаще выявлялись повышенные уровни ЛДГ, гомоцистеина, СРБ и D-димера, а также дефицит витамина D ($p<0,05$). По данным однофакторного анализа, наибольшую прогностическую значимость имели ЛДГ (OR=3,8), гомоцистеин (OR=3,5) и СРБ (OR=2,4). В многофакторной модели независимыми предикторами преэклампсии оставались повышенный уровень ЛДГ и гипергомоцистеинемия. Допплерометрические признаки повышения сосудистого сопротивления в маточных артериях усиливали точность прогнозирования.

Заключение. Комплексная оценка биохимических и допплерометрических показателей позволяет эффективно выявлять группу высокого риска развития преэклампсии у беременных после ЭКО и обосновывает необходимость раннего профилактического вмешательства.

Ключевые слова: экстракорпоральное оплодотворение, преэклампсия, прогнозирование, биомаркеры, гемостаз, допплерометрия.

Введение

Преэклампсия остается одной из ведущих причин материнской и перинатальной заболеваемости и смертности во всем мире. Беременности, наступившие в результате вспомогательных репродуктивных технологий, в частности экстракорпорального оплодотворения (ЭКО), характеризуются повышенным риском развития гипертензивных осложнений по сравнению со спонтанным зачатием. В основе данного риска лежат нарушения имплантации и плацентации, эндотелиальная дисфункция, иммуновоспалительная активация и дисбаланс системы гемостаза.

Современные исследования указывают на высокую прогностическую ценность биохимических маркеров, отражающих процессы воспаления, окислительного стресса и коагуляции. Допплерометрическая оценка маточных артерий позволяет объективизировать степень нарушения маточно-плацентарного кровотока и является важным инструментом раннего скрининга плацентарной недостаточности.

Несмотря на накопленные данные, вопросы комплексного прогнозирования преэклампсии у беременных после ЭКО остаются недостаточно изученными. Формирование интегрированных моделей риска представляет собой актуальную научно-практическую задачу, направленную на повышение эффективности профилактики и снижение частоты тяжелых акушерских осложнений.

Цель исследования — оценить прогностическую значимость клинико-лабораторных и допплерометрических показателей в развитии преэклампсии у беременных после ЭКО.

Introduction

Preeclampsia is one of the leading causes of maternal and perinatal morbidity and mortality worldwide and remains a major challenge in modern obstetrics. The condition is characterized by new-onset hypertension and multisystem involvement after 20 weeks of gestation and is associated with severe maternal complications, fetal growth restriction, preterm birth and increased perinatal mortality.

In recent decades, the widespread use of assisted reproductive technologies, particularly in vitro fertilization (IVF), has significantly increased the number of pregnancies achieved through artificial conception. Numerous epidemiological studies and meta-analyses have demonstrated that pregnancies after IVF are associated with a higher risk of hypertensive disorders, including preeclampsia, compared with spontaneous conception. The increased risk is attributed to altered implantation processes, abnormal placentation, immune maladaptation, endothelial dysfunction and epigenetic factors.

Placental ischemia and impaired trophoblastic invasion lead to the release of antiangiogenic and inflammatory mediators, resulting in systemic endothelial dysfunction and generalized vasoconstriction. Biomarkers reflecting oxidative stress, tissue damage, inflammation and coagulation activation have therefore attracted considerable attention as potential early predictors of preeclampsia. Elevated lactate dehydrogenase (LDH) reflects cellular hypoxia and oxidative injury, while hyperhomocysteinemia contributes to endothelial damage and vascular dysfunction. C-reactive protein (CRP) is a sensitive marker of systemic inflammation and has been associated with the severity of hypertensive disorders of pregnancy. Increased D-dimer levels indicate activation of the coagulation cascade and microthrombotic processes in the placental circulation. Vitamin D deficiency has been implicated in immune dysregulation, impaired placental development and increased cardiovascular risk.

In addition to laboratory markers, Doppler ultrasound assessment of uterine artery blood flow provides valuable information about placental perfusion and vascular resistance. Increased pulsatility and resistance indices in early pregnancy reflect impaired uteroplacental circulation and have been associated with subsequent development of preeclampsia and fetal growth restriction.

Despite the availability of individual biomarkers and ultrasound parameters, there is no universally accepted predictive model for preeclampsia in IVF pregnancies. Most existing screening algorithms are derived from spontaneously conceived pregnancies and may not fully reflect the specific pathophysiological

mechanisms in assisted reproduction. Therefore, the development of integrated predictive approaches combining biochemical and Doppler parameters is of particular clinical importance.

Early identification of high-risk patients enables timely implementation of preventive strategies, including low-dose aspirin therapy, correction of modifiable risk factors, individualized antenatal surveillance and optimization of perinatal care. Improving predictive accuracy in IVF pregnancies may significantly reduce the burden of severe obstetric complications and improve maternal and neonatal outcomes.

The aim of this study was to evaluate the predictive value of clinical, biochemical and Doppler parameters for the development of preeclampsia in pregnant women after in vitro fertilization.

Materials and Methods

A prospective observational study was conducted from 2023 to 2025 at the **Bukhara State Maternity Complex**. The study included 80 pregnant women after in vitro fertilization (IVF) and 40 women with spontaneous singleton pregnancies who formed the control group.

Inclusion criteria: singleton pregnancy after IVF, gestational age of 11–14 weeks at enrollment, written informed consent. **Exclusion criteria:** chronic arterial hypertension, pregestational diabetes mellitus, autoimmune diseases, chronic kidney disease, multiple pregnancy and congenital fetal anomalies.

According to pregnancy outcomes, women after IVF were divided into two subgroups:

- **Group 1 (n=24):** patients who developed preeclampsia during pregnancy.
- **Group 2 (n=56):** patients with uncomplicated pregnancy after IVF.

Blood samples were collected at 11–14 weeks of gestation. Serum concentrations of lactate dehydrogenase (LDH), homocysteine, C-reactive protein

(CRP), D-dimer and vitamin D were determined using enzyme-linked immunosorbent assay and standard biochemical methods. Coagulation parameters including activated partial thromboplastin time (APTT), fibrinogen, prothrombin index and international normalized ratio (INR) were assessed.

Doppler ultrasound examination of uterine arteries was performed using an expert-class ultrasound system with calculation of pulsatility index (PI), resistance index (RI) and systolic/diastolic ratio (S/D).

Statistical analysis was performed using SPSS software. Quantitative variables were expressed as mean ± standard deviation. Group comparisons were performed using Student's t-test or Mann–Whitney U test depending on data distribution. Categorical variables were analyzed using the χ^2 test. Odds ratios (OR) with 95% confidence intervals (CI) were calculated. Multivariate logistic regression analysis was applied to identify independent predictors of preeclampsia. A p-value <0.05 was considered statistically significant.

Results

A total of 80 pregnant women after IVF and 40 women with spontaneous pregnancies were analyzed. The mean age of patients in the IVF group was 33.6 ± 4.2 years and did not significantly differ from the control group (32.9 ± 3.8 years, p>0.05). The incidence of preeclampsia in the IVF group was 30% (24/80).

Women who subsequently developed preeclampsia demonstrated significantly higher serum levels of LDH, homocysteine, CRP and D-dimer compared with women with uncomplicated IVF pregnancies and controls (p<0.05). Vitamin D levels were significantly lower in the preeclampsia group (p<0.05).

Elevated LDH (>357 U/L) was associated with a markedly increased risk of preeclampsia (OR = 3.88; 95% CI 1.56–9.65; p = 0.003). Hyperhomocysteinemia (>17 μmol/L) also significantly increased the risk (OR = 3.55; 95% CI 1.49–8.45; p = 0.004). Increased D-dimer levels (>872 ng/mL) were associated with higher odds of preeclampsia (OR = 2.33; 95% CI 1.03–5.30; p = 0.041). Elevated CRP (>8 mg/L) showed a significant association with disease development (OR = 2.49;

95% CI 1.06–5.86; p = 0.035). Vitamin D deficiency (<20 ng/mL) demonstrated a trend toward increased risk, although statistical significance was not reached in multivariate analysis.

Doppler ultrasound assessment revealed increased uterine artery pulsatility and resistance indices in patients who later developed preeclampsia, indicating impaired uteroplacental perfusion ($p<0.05$).

Multivariate logistic regression identified elevated LDH and homocysteine as independent predictors of preeclampsia, while CRP and D-dimer contributed additional predictive value to the combined model. The integrated model demonstrated satisfactory discriminative ability for early prediction of preeclampsia

Discussion

The present study demonstrates that pregnancies achieved by in vitro fertilization are characterized by a relatively high incidence of preeclampsia, confirming previously reported data on increased obstetric risk in this population. The identified associations between biochemical markers and subsequent development of preeclampsia highlight the multifactorial nature of this complication, involving endothelial dysfunction, inflammatory activation and coagulation imbalance.

Elevated LDH reflects cellular damage, oxidative stress and placental hypoxia, which are key mechanisms in the pathogenesis of preeclampsia. Hyperhomocysteinemia contributes to endothelial injury, impaired nitric oxide synthesis and increased vascular resistance, thereby promoting placental ischemia. Increased CRP levels indicate systemic inflammatory activation, which has been widely implicated in the progression of hypertensive disorders of pregnancy. Elevated D-dimer reflects activation of the coagulation cascade and microthrombotic processes within the placental circulation.

Vitamin D deficiency, although not an independent predictor in multivariate analysis, demonstrated an association with increased risk of preeclampsia, which is

consistent with data suggesting its role in immune modulation and vascular function.

Doppler findings indicating increased uterine artery resistance further support the presence of impaired placental perfusion in high-risk patients. The combination of laboratory biomarkers with Doppler ultrasound parameters improves predictive accuracy and allows earlier identification of patients requiring intensified surveillance and preventive interventions.

The results of this study emphasize the clinical relevance of integrated screening strategies in IVF pregnancies. Early recognition of high-risk patients may facilitate timely initiation of preventive measures, including low-dose aspirin therapy, correction of vitamin D deficiency and closer antenatal monitoring.

Conclusion

Elevated serum levels of lactate dehydrogenase and homocysteine are independent predictors of preeclampsia in pregnant women after IVF. Increased CRP, D-dimer and altered uterine artery Doppler indices further enhance predictive accuracy. Combined assessment of biochemical and Doppler parameters allows early stratification of patients according to preeclampsia risk and supports personalized preventive strategies aimed at improving maternal and perinatal outcomes.

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