INTEGRATION OF CLINICAL AND IMMUNOLOGICAL PARAMETERS FOR PREECLAMPSIA RISK STRATIFICATION

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Abstract

Beyond immune-inflammatory mechanisms, premorbid somatic factors play a significant role in the pathogenesis of preeclampsia (PE); however, their contribution to cytokine imbalance and clinical severity remains insufficiently explored. Cardiovascular pathology, dyslipidemia, and a positive family history of PE may potentiate systemic inflammation and exacerbate gestational complications. This prospective study included 150 pregnant women (120 with PE and 30 uncomplicated pregnancies). Within the PE group, subgroups were defined based on the presence of pre-existing arterial hypertension, obesity/dyslipidemia, and family history of PE. Multiplex cytokine assays (IL-2, IL-4, IL-6, IL-8, IL-10, GM-CSF, IFN-γ, TNF-α) were performed with calculation of integrated cytokine ratios. The risk of PE was assessed using multivariate logistic regression. The presence of two or more risk factors was associated with significantly higher pro-inflammatory cytokines, earlier PE onset, more severe disease, and poorer perinatal outcomes. A combined clinical-immunological model (≥2 risk factors + TNF-α/IL-10 >2.5) showed high predictive performance for severe PE (AUC=0.91). Incorporating these clinical parameters into comprehensive risk assessment alongside cytokine biomarkers enables more accurate patient stratification and timely adjustment of obstetric management.

Keywords. *preeclampsia, risk stratification, cardiovascular diseases, dyslipidemia, family history, cytokines, TNF-α/IL-10 ratio, systemic inflammation, pregnancy outcomes, comorbid risk factors.*

Aim of the study. To evaluate the impact of chronic cardiovascular diseases, lipid metabolism disorders, and a positive family history of preeclampsia on the risk of PE development, as well as their association with the magnitude of cytokine imbalance and adverse maternal and perinatal outcomes.

Material and methods of research. This prospective study included 150 pregnant women (120 with PE and 30 with uncomplicated pregnancies). Within the PE group, subgroups were defined based on the presence of somatic risk factors: pre-existing arterial hypertension, obesity/dyslipidemia (total cholesterol >6.5 mmol/L, triglycerides >2.3 mmol/L), and a family history of PE (in mothers or sisters). Multiplex cytokine assays (IL-2, IL-4, IL-6, IL-8, IL-10, GM-CSF, IFN-γ, TNF-α) were performed with calculation of integrated cytokine ratios [9]. The risk of PE was assessed using multivariate logistic regression analysis [1,3]. All patients provided written informed consent.

Results and discussion. The incidence of PE was significantly higher in women with two or more concomitant risk factors: cardiovascular disease was associated with a 2.1-fold increased risk (OR 2.1; 95% CI 1.4–3.2), dyslipidemia with a 1.8-fold increased risk (OR 1.8; 95% CI 1.2–2.7), and a positive family history with a 2.4-fold increased risk (OR 2.4; 95% CI 1.6–3.6) [5,6]. In the PE group with these factors, pro-inflammatory cytokine levels (TNF-α, IL-6, IFN-γ) were significantly higher, while IL-10 levels were lower compared to PE patients without these comorbidities ($p<0.01$). The most pronounced shifts were observed when all three factors coexisted: TNF-α reached 32.4 [24.1; 41.2] pg/mL versus 18.6 [14.2; 23.9] pg/mL in the factor-free group ($p<0.001$); the TNF-α/IL-10 ratio peaked at 7.8 [5.9; 10.2]. Moreover, the presence of these somatic predictors was associated with earlier PE onset (<34 weeks in 68.4% vs. 31.6%, $p=0.002$), a higher rate of severe PE (81.3% vs. 45.6%, $p<0.001$), and poorer perinatal outcomes (mean neonatal birth weight 1840±410 g vs. 2780±490 g, $p<0.001$) [7,8]. ROC analysis demonstrated that a combined model (presence of ≥2 risk factors + TNF-α/IL-10 >2.5) exhibited high predictive performance for severe PE (AUC=0.91, sensitivity 89%, specificity 84%). These findings confirm that somatic comorbidities not only increase the risk of PE but also amplify the inflammatory response, which is consistent with the two-stage model of preeclampsia [2,4].

Conclusions. Cardiovascular diseases, lipid metabolism disorders, and a positive family history of PE are independent risk factors for the development of preeclampsia, and their combined presence significantly amplifies the pro-inflammatory cytokine response and worsens pregnancy outcomes. Incorporating these clinical parameters into comprehensive risk assessment alongside cytokine biomarkers enables more accurate patient stratification and timely adjustment of obstetric management strategies [10].

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