CYTOKINE PROFILE IMBALANCE IN PREECLAMPSIA: ASSOCIATION WITH GESTATIONAL AGE AT ONSET AND PERINATAL OUTCOMES

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Abstract

Preeclampsia (PE) is a leading cause of maternal and perinatal morbidity, with immune dysregulation and a shift toward the pro-inflammatory Th1 phenotype considered key pathogenetic mechanisms. However, the temporal dynamics of this imbalance across different gestational ages remain insufficiently characterized. This prospective comparative study included 150 pregnant women (120 with PE, 30 uncomplicated controls). PE patients were stratified by gestational age at onset: <34 weeks, 34–36 weeks, and ≥37 weeks. Plasma concentrations of IL-2, IL-4, IL-6, IL-8, IL-10, GM-CSF, IFN-γ, and TNF-α were measured using multiplex assay; integrated cytokine ratios (TNF-α/IL-10, IFN-γ/IL-4, IL-2/IL-4) were calculated. All PE patients exhibited a pronounced cytokine imbalance, with the most substantial alterations in early-onset PE (<34 weeks). Integrated ratios showed greater discriminatory capacity than absolute cytokine values. TNF-α/IL-10 ratio correlated negatively with neonatal birth weight, and was a strong predictor of severe PE and preterm delivery (AUC=0.87). Assessment of the cytokine profile, particularly a TNF-α/IL-10 ratio threshold >2.5, may serve as an adjunctive objective criterion for risk stratification and for guiding the timing of therapeutic intervention and delivery in pregnancies complicated by preeclampsia.

Keywords. *preeclampsia, cytokine profile, Th1/Th2 imbalance, TNF-α/IL-10 ratio, gestational age, perinatal outcomes, early-onset preeclampsia, systemic inflammation, risk stratification, preterm delivery.*

Aim of the study. To evaluate the changes in plasma levels of pro- and anti-inflammatory cytokines in women with preeclampsia at various gestational ages and to assess their prognostic value for maternal and perinatal outcomes.

Material and methods of research. A prospective comparative study was conducted involving 150 pregnant women, divided into a PE group (n=120) and a control group with uncomplicated pregnancies (n=30). Patients with PE were stratified by gestational age at disease onset: <34 weeks, 34–36 weeks, and ≥37 weeks. Plasma concentrations of IL-2, IL-4, IL-6, IL-8, IL-10, GM-CSF, IFN-γ, and TNF-α were measured using multiplex assay (xMAP technology) [7,9]. Integrated cytokine ratios (TNF-α/IL-10, IFN-γ/IL-4, IL-2/IL-4) were calculated. Statistical analysis included non-parametric tests, Spearman's correlation, and ROC-curve analysis [1,4]. All patients provided written informed consent.

Results and discussion. All PE patients exhibited a pronounced cytokine imbalance characterized by elevated pro-inflammatory cytokines (IL-6, TNF-α, IFN-γ) and reduced anti-inflammatory cytokines (IL-10, IL-4) compared to controls ($p<0.001$) [3,8]. The

most substantial alterations were observed in the early-onset PE subgroup (<34 weeks). Integrated ratios demonstrated greater discriminatory capacity than absolute cytokine values. TNF-α levels correlated positively with mean arterial pressure (r=0.62), IL-6 correlated with PE severity (r=0.58), and the TNF-α/IL-10 ratio showed a negative correlation with neonatal birth weight (r=−0.54) [2,5]. In the early-onset PE subgroup, severe PE was recorded in 72.5% of cases, and admission to the neonatal intensive care unit occurred in 67.5%, significantly exceeding the rates in late-onset PE. ROC analysis revealed that the TNF-α/IL-10 ratio was a strong predictor of severe PE and preterm delivery (AUC=0.87) [6,10]. These findings confirm that the pro-inflammatory shift is more pronounced in early-onset disease, which is consistent with the two-stage model of preeclampsia and may reflect a more severe underlying placental pathology [2,4].

Conclusions. The magnitude of the pro-inflammatory shift in PE is inversely related to gestational age at disease manifestation. Assessment of the cytokine profile, particularly a TNF-α/IL-10 ratio threshold >2.5, may serve as an adjunctive objective criterion for risk stratification and for guiding the timing of therapeutic intervention and delivery in pregnancies complicated by preeclampsia [1,3,8].

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