SERUM VEGF-A AND IL-17A AS BIOMARKERS FOR EARLY PREGNANCY LOSS RISK ASSESSMENT

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Abstract: *Early pregnancy loss remains one of the leading complications of first-trimester gestation, affecting approximately 10–18% of clinically recognized pregnancies. Emerging evidence suggests that dysregulation of angiogenic and inflammatory pathways contributes significantly to impaired placentation and embryonic demise. This study aimed to evaluate the clinical significance of serum VEGF-A and IL-17A levels, as well as their ratio, in women with threatened miscarriage and early spontaneous abortion. A prospective analysis was conducted among 96 pregnant women at 6–11 weeks of gestation. Serum cytokine levels were measured using multiplex immunoassay, and hormonal markers were assessed via ELISA. Women who experienced spontaneous abortion demonstrated significantly elevated VEGF-A levels and reduced IL-17A concentrations compared to those with preserved pregnancies. The VEGF-A/IL-17A ratio was strongly associated with decreased progesterone levels and increased miscarriage risk (OR=2.3, 95% CI 1.5–3.4). Multivariate modeling demonstrated high predictive performance (AUC=0.87). These findings suggest that angiogenic–immunological imbalance may serve as a potential biomarker system for early pregnancy loss risk assessment.*

Keywords: *early pregnancy loss, VEGF-A, IL-17A, cytokines, angiogenesis, threatened miscarriage, biomarkers.*

Introduction

First-trimester miscarriage represents a major challenge in reproductive medicine. Although chromosomal abnormalities account for a significant proportion of cases, immunological and vascular dysfunctions are increasingly recognized as critical contributors to pregnancy failure. Successful implantation and early placental development require tightly regulated angiogenesis and immune tolerance.

Vascular endothelial growth factor A (VEGF-A) plays a central role in placental vascular remodeling, while interleukin-17A (IL-17A), a pro-inflammatory cytokine secreted by Th17 cells, modulates immune responses at the maternal–fetal interface. An imbalance between angiogenic signaling and immune regulation may disrupt trophoblast invasion and decidualization processes.

This study investigates whether alterations in VEGF-A and IL-17A serum levels, individually and in combination, are associated with early pregnancy loss and whether their ratio may serve as a predictive clinical marker.

Materials and Methods

A prospective observational study was conducted at a tertiary perinatal center between 2023 and 2024. Ninety-six pregnant women aged 19–39 years with singleton intrauterine pregnancies at 6–11 weeks of gestation were included.Participants were categorized into three groups:

- Normal Pregnancy (NP): n = 58

- Threatened Miscarriage with Ongoing Pregnancy (TM-OP): n = 22
- Threatened Miscarriage with Subsequent Abortion (TM-SA): n = 16

Exclusion criteria included progesterone therapy prior to sampling, assisted reproductive technologies, multiple gestation, severe hemorrhage, known autoimmune disorders, and incomplete clinical data.

Laboratory Assessment

Serum levels of VEGF-A, IL-17A, IL-2, and TNF-α were measured using multiplex bead-based immunoassay. Progesterone, human chorionic gonadotropin (hCG), and estradiol were evaluated by ELISA. Complete blood count and cytogenetic screening were performed.

Statistical Analysis

Data were expressed as mean ± standard deviation. Group comparisons were conducted using Student's t-test and ANOVA. Multivariate logistic regression and partial least squares regression (PLSR) analyses were applied. Statistical significance was set at $p < 0.05$.

Results

Women in the TM-SA group demonstrated significantly higher VEGF-A levels (8.10 ± 2.40 pg/mL) compared to TM-OP (5.90 ± 2.10 pg/mL) and NP groups (6.00 ± 2.30 pg/mL). Conversely, IL-17A levels were significantly reduced in TM-SA (6.20 ± 2.10 pg/mL) compared to TM-OP (8.40 ± 1.90 pg/mL).The VEGF-A/IL-17A ratio was markedly elevated in TM-SA (1.31 vs. 0.74 in NP, $p < 0.001$). Correlation analysis revealed a negative association between this ratio and progesterone levels ($r = -0.39$).Hormonal analysis showed significantly decreased progesterone (26.8 ± 15.2 nmol/L), hCG

(14,200 ± 4,500 IU/L), and estradiol (210 ± 75 pg/mL) in the TM-SA group. Leukocyte counts were elevated (12.8 ± 3.1 $\times 10^9$/L), indicating inflammatory activation.

Multivariate logistic regression identified VEGF-A/IL-17A ratio as an independent predictor of miscarriage risk. Each 0.5-unit increase in the ratio was associated with a 2.3-fold higher risk of spontaneous abortion (95% CI 1.5–3.4). Reduced progesterone and IL-17A levels were also independent risk factors.The model demonstrated strong predictive performance with AUC=0.87 (95% CI 0.79–0.94).PLSR analysis clearly distinguished groups (Q^2=0.84, $p<0.001$), confirming combined effects of angiogenic and immune parameters.

Discussion

The findings highlight the interplay between angiogenesis and immune regulation in early pregnancy maintenance. Elevated VEGF-A in the presence of reduced IL-17A suggests compensatory vascular activation alongside impaired immune modulation. The observed association between VEGF-A/IL-17A imbalance and progesterone deficiency further supports the concept of endocrine–immune interaction in miscarriage pathogenesis.

The predictive performance of the VEGF-A/IL-17A ratio underscores its potential clinical utility as an early biomarker. Integration of immunological and hormonal indicators may enhance early risk stratification strategies.

Conclusion

An imbalance between VEGF-A and IL-17A is significantly associated with early pregnancy loss. The VEGF-A/IL-17A ratio may serve as a clinically relevant biomarker for early detection of miscarriage risk and may support personalized monitoring strategies in reproductive medicine.

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