

**PREDICTIVE RELEVANCE OF IL-10/TNF α RATIO FOR
EARLY PREGNANCY LOSS**

Yaqubova Muyassar Dilmurod qizi – PhD Candidate

Tashkent State Medical University (Tashkent, Uzbekistan)

Muminova Ziyoda Abrorovna – MD, PhD, Associate Professor

Tashkent State Medical University (Tashkent, Uzbekistan)

Abstract: *Pregnancy requires finely tuned maternal immune adaptations to tolerate the semi-allogeneic fetus while maintaining protection against infection. Among key mediators, interleukin-10 (IL-10) supports immune tolerance and suppresses excessive inflammation, whereas tumor necrosis factor- α (TNF α) promotes pro-inflammatory responses. To evaluate the dynamics of IL-10 and TNF α during early pregnancy and to assess the clinical value of the IL-10/TNF α ratio as a potential indicator of pregnancy outcome, including the influence of advanced maternal age. A prospective observational study was conducted in 2023–2024 at a tertiary obstetric center in Tashkent. A total of 98 pregnant women were included: 76 women with a history of prior pregnancy loss and 22 healthy pregnant women. Serum IL-10 and TNF α levels were assessed during the first trimester using immunoassay methods. In pregnancies complicated by early loss, IL-10 failed to rise and showed a downward trend, while TNF α increased relative to controls. At 6–8 weeks, mean IL-10 was 2.66 ± 0.81 pg/mL in controls versus 2.21 ± 0.74 pg/mL in the study group ($p < 0.05$), whereas TNF α was 5.33 ± 1.40 pg/mL versus 6.11 ± 1.44 pg/mL, respectively ($p < 0.05$). The IL-10/TNF α ratio at 6–8 weeks was lower in the study group (0.37 ± 0.12) compared with controls (0.52 ± 0.18 , $p < 0.01$). The IL-10/TNF α ratio reflects the balance between immune tolerance and inflammation in early pregnancy and may serve as a practical immunological*

indicator for identifying women at increased risk of adverse outcomes, particularly among older mothers and those with prior pregnancy losses.

Keywords: pregnancy immunology, IL-10, TNF α , cytokines, miscarriage, immune tolerance, IL-10/TNF α ratio.

Introduction

Pregnancy is an immunologically unique condition requiring maternal adaptation to the semi-allogeneic fetus. Classical models describe a shift toward anti-inflammatory dominance, especially during early gestation, to support implantation and placental development. Cytokines serve as central signaling mediators in this adaptation. IL-10 is a major anti-inflammatory cytokine supporting immune tolerance, while TNF α contributes to pro-inflammatory activity; excessive TNF α has been linked to miscarriage risk and placental dysfunction. Therefore, the IL-10/TNF α ratio has gained interest as a composite marker reflecting the overall immune milieu rather than isolated cytokine values.

Materials and Methods

This prospective study included 98 pregnant women observed in the first trimester. The study group consisted of women with a prior history of pregnancy loss ($n=76$), and the control group included healthy pregnant women without adverse reproductive history ($n=22$). Serum IL-10 and TNF α were measured during early gestation, and participants were additionally categorized by maternal age (<35 and ≥ 35 years). Data were analyzed with standard comparative statistics; $p<0.05$ was considered significant.

Results

In the control group, IL-10 demonstrated a progressive rise from early to late first trimester, while TNF α remained stable or slightly decreased. In contrast, in the study group, IL-10 values were consistently lower and tended to decline in pregnancies with adverse evolution, whereas TNF α showed a

relative increase. At 6–8 weeks, the IL-10/TNF α ratio was significantly reduced in the study group (0.37 ± 0.12) compared with controls (0.52 ± 0.18), indicating a shift toward a pro-inflammatory immune profile. Age-based stratification suggested that women ≥ 35 years had lower IL-10 concentrations and a reduced IL-10/TNF α ratio, consistent with diminished anti-inflammatory potential in advanced maternal age. TNF α values did not differ significantly between age groups, suggesting that reduced anti-inflammatory response rather than excessive TNF α production may underlie age-related immune alterations.

Discussion

The findings confirm that early pregnancy viability is strongly associated with balanced cytokine regulation. A progressive rise in IL-10 during early gestation appears to support maternal–fetal immune tolerance, whereas insufficient IL-10 elevation may predispose to inflammatory dominance. The reduced IL-10/TNF α ratio observed in pregnancies with adverse outcomes suggests a shift toward a pro-inflammatory profile. This imbalance may disrupt trophoblast invasion, placental development, and vascular remodeling processes necessary for pregnancy continuation. The association between advanced maternal age and lower IL-10 levels further highlights the role of age-related immune modulation in pregnancy risk. Although TNF α levels did not significantly increase with age, the decline in IL-10 may shift the immunological equilibrium toward a relatively inflammatory state. From a clinical perspective, monitoring the IL-10/TNF α ratio in early pregnancy could provide additional prognostic information, especially in women with prior pregnancy loss or advanced maternal age.

Conclusion

The findings support that early pregnancy success is closely linked to the immune balance between IL-10 and TNF α . The IL-10/TNF α ratio may serve as an accessible biomarker for early risk stratification and individualized monitoring, particularly in women with prior pregnancy losses and in advanced

maternal age. Future studies should integrate cytokine ratios with clinical predictors and evaluate their performance in predictive models.

REFERENCES

1. Brogin Moreli, J., Cirino Ruocco, A. M., Vernini, J. M., Rudge, M. V. C., & Calderon, I. M. P. (2012). Interleukin-10 and tumor necrosis factor-alpha in pregnancy: Aspects of interest in clinical obstetrics. *International Scholarly Research Notices*, 2012, 230742.
2. Yaqubova M, et al. Risk Assessment of Reproductive Losses in the First Trimester of Pregnancy: A Logistic Regression Model Based on IL-10. *American Journal of Medicine and Medical Sciences*. 2025;15(8)
3. Kaislasuo, J., et al. (2020). IL-10 to TNF α ratios throughout early first trimester can discriminate healthy pregnancies from pregnancy losses. *American Journal of Reproductive Immunology*, 83(1), e13195.
4. Lean, S. C., et al. (2021). A prospective cohort study providing insights for markers of adverse pregnancy outcome in older mothers. *BMC Pregnancy and Childbirth*, 21, 1–17.
5. Raghupathy, R. (2022). Cytokines and pregnancy complications: Modulation for prevention and treatment. *Exploration of Immunology*, 2(3), 414–427.