Volume 3, Issue 3, March - 2025 **ISSN (E):** 2938-3811

Web of Scientists and Scholars: Journal of Multidisciplinary Research

IMPACT OF TIMELY ANTIMICROBIAL THERAPY FOR URINARY TRACT INFECTIONS ON PREECLAMPSIA: A PROSPECTIVE OBSERVATIONAL STUDY

Radjabova Zulola Abduhakimovna
ORCID: 0009-0008-9408-9312

Saipova Dinora Azatovna
ORCID: 0009-0008-1505-8957

Radjabova Nazokat Shukhratovna
ORCID: 0009-0008-9408-9312
Center for the Development of Professional Skills of Medical Workers, Tashkent

Abstract
Preeclampsia (PE) is one of the most significant complications of pregnancy, associated with a high risk of maternal and perinatal morbidity and mortality. According to current data, PE develops in 2–8% of pregnant women and remains one of the leading causes of antenatal hospitalization, preterm birth, and obstetric interventions. Of particular interest is the comparison between expectant management and prophylactic treatment, especially when paucisymptomatic forms of UTI are detected in the first or second trimesters.

Introduction

Preeclampsia (PE) is one of the most significant complications of pregnancy, associated with a high risk of maternal and perinatal morbidity and mortality. According to current data, PE develops in 2–8% of pregnant women and remains one of the leading causes of antenatal hospitalization, preterm birth, and obstetric interventions [1,2]. Despite progress in understanding the pathogenesis of PE—including angiogenic imbalance, endothelial dysfunction, and impaired placentation—its clinical prevention remains limited, and therapeutic approaches are still predominantly symptomatic [3]. Urinary tract infections (UTIs), including asymptomatic bacteriuria, are considered one of the potential exogenous factors capable of inducing mechanisms involved in PE development. As shown in several studies, UTIs activate pro-inflammatory cascades (via Interleukin-6 [IL-6], Tumor Necrosis Factor-alpha [TNF-α], C-Reactive Protein [CRP]), disrupt the angiogenic balance (increased soluble fms-like tyrosine kinase-1 [sFlt-1], decreased Placental Growth Factor [PlGF]), and contribute to vascular dysfunction—all key links in the pathogenesis of PE [4,5]. The problem is compounded by the fact that asymptomatic UTIs can remain undiagnosed for extended periods, particularly in settings with low coverage of microbiological screening. Due to limited laboratory resources or the practice of expectant management, a proportion of pregnant women with bacteriuria do not receive timely treatment, which may increase the risk of preeclampsia or exacerbate its course [6,7]. Nevertheless, despite a theoretically plausible link between UTIs

and PE, data on the impact of timely antimicrobial therapy on the risk and severity of PE remain limited and contradictory. Specifically, it is currently unclear: whether early antibacterial therapy (before 20–22 weeks of gestation) reduces the risk of PE; whether treatment of asymptomatic bacteriuria affects the incidence of severe forms of PE; whether microbiological data and treatment factors can be used to develop prognostic models.

Of particular interest is the comparison between expectant management and prophylactic treatment, especially when paucisymptomatic forms of UTI are detected in the first or second trimesters. Given the rise in antibiotic resistance and the need for rational antimicrobial prescribing, this issue requires a rigorously evidence-based approach based on prospective observational data.

The aim of this study was to evaluate the impact of timely antimicrobial therapy for UTIs on the incidence and severity of preeclampsia in a cohort of pregnant women, followed by an analysis of prognostic factors and the development of statistical risk assessment models (Receiver Operating Characteristic [ROC] analysis, logistic regression).

Materials and Methods

A prospective cohort observational study was conducted to investigate the impact of timely antimicrobial therapy for urinary tract infections (UTIs) on the incidence and severity of preeclampsia (PE) in pregnant women. The study was carried out in two specialized perinatal centers in Uzbekistan from January 1, 2022, to December 31, 2024. A total of 456 pregnant women who presented at a gestational age of up to 20 weeks and were diagnosed with a UTI at the initial examination (based on urinalysis and/or urine culture) were enrolled. The women were allocated into two cohort groups: Group 1 (n=227) received timely etiotropic treatment (antibiotics within 48–72 hours after diagnosis); Group 2 (n=229) experienced delayed therapy (initiated ≥10 days after laboratory confirmation of UTI) or did not receive immediate therapy for various reasons (patient refusal, delayed culture results, physician's expectant management strategy).

Inclusion Criteria: Gestational age ≤20 weeks at the time of UTI detection; Confirmed bacteriuria $\geq 10^5$ Colony Forming Units (CFU)/mL in urine culture; Absence of signs of preeclampsia at enrollment; Willingness to participate in follow-up until delivery.

Exclusion Criteria: Chronic kidney disease, autoimmune or systemic inflammatory diseases; Type 1 or Type 2 diabetes mellitus, gestational diabetes; Multiple pregnancy; History of PE in previous pregnancies; Smoking, substance abuse; Antibiotic therapy within 14 days prior to enrollment.

Diagnosis and Confirmation of UTI. UTI was diagnosed based on: a positive urinalysis (leukocyturia >10 cells per high-power field [HPF], positive nitrite test, proteinuria); confirmed bacteriuria $\geq 10^5$ CFU/mL; for asymptomatic bacteriuria – absence of clinical manifestations (pain, fever, dysuria).

All participants underwent: urine culture with pathogen identification and antimicrobial susceptibility testing; complete blood count (leukocytes, CRP, Erythrocyte Sedimentation Rate

[ESR]); renal ultrasound (if indicated); monthly monitoring of blood pressure (BP) and proteinuria; and follow-up until 38 weeks of gestation.

Recommended first-line drugs, considering microbial susceptibility, were used for treatment: fosfomycin trometamol (3 g single dose) for asymptomatic bacteriuria; nitrofurantoin 100 mg twice daily for 5–7 days; cephalexin 500 mg twice daily for 7 days; amoxicillin/clavulanate 625 mg twice daily (if susceptible). The choice of antibiotic was coordinated with an obstetrician-gynecologist and a clinical pharmacologist. Management of both groups adhered to clinical protocols.

Outcomes and Assessment Criteria. Primary outcomes: Incidence of preeclampsia (any severity); Onset of preeclampsia (early <34 weeks or late ≥34 weeks); Incidence of severe PE (BP ≥160/110 mmHg, HELLP syndrome, eclampsia).

Secondary outcomes: Incidence of preterm birth; Fetal birth weight; Incidence of neonatal intensive care unit (NICU) admission; Rate of cesarean sections for obstetric indications.

Statistical Analysis. Statistical analysis was performed using SPSS Statistics v.27 and MedCalc v.22. Normality of distribution was assessed using the Shapiro-Wilk test. Frequencies were compared using the χ^2 test or Fisher's exact test. Quantitative variables were compared using Student's t-test (or Mann-Whitney U test for non-normally distributed data). The association between UTI treatment and outcomes was analyzed using logistic regression (Odds Ratio [OR], 95% Confidence Interval [CI]). Receiver Operating Characteristic (ROC) analysis was used to assess the prognostic value of early treatment (Area Under the Curve [AUC], sensitivity, specificity). A p-value <0.05 was considered statistically significant.

Results

A total of 456 pregnant women with laboratory-confirmed UTIs were included in the study. The mean age of the women was 27.3 ± 4.9 years. Both groups were comparable in terms of age, parity, gestational age at enrollment, body mass index (BMI), and ESR/CRP levels at diagnosis (p>0.05 for all parameters).

Incidence of Preeclampsia and its Severe Forms. Preeclampsia developed in 42 (18.5%) women in the immediate treatment group (Group 1) and in 79 (34.5%) women in the delayed treatment group (Group 2) (p<0.001). Severe PE occurred in 11 cases (4.8%) in Group 1 and 33 cases (14.4%) in Group 2 (p=0.002). Thus, timely UTI treatment was associated with a 46% reduction in the overall incidence of PE and a more than 2.5-fold reduction in severe forms. Logistic regression analysis showed that delayed UTI treatment increased the risk of PE independently of age, gestational age at enrollment, and BMI.

To assess the predictive significance of timely UTI treatment in preventing PE, ROC analysis was performed. A model including variables (UTI treatment status, age, and presence of asymptomatic bacteriuria) demonstrated high prognostic accuracy. The AUC was 0.78 (95% CI: 0.72–0.83), with a sensitivity of 76%, specificity of 69%, and Youden's Index of 0.45.

Thus, early UTI treatment demonstrates good prognostic value in reducing the risk of PE, particularly its severe and early-onset forms.

Conclusion

Timely antimicrobial therapy for UTIs, initiated within the first 72 hours after laboratory verification, statistically significantly reduces the incidence of preeclampsia in pregnant women, including its severe forms. Logistic regression and ROC analysis confirmed the predictive significance of early treatment. These findings support the need for routine microbiological screening and prompt initiation of therapy upon detection of UTIs in early pregnancy.

References

1. American College of Obstetricians and Gynecologists. Gestational Hypertension and Preeclampsia: ACOG Practice Bulletin No. 222. Obstet Gynecol. 2020;135(6):e237–e260. doi:10.1097/AOG.003891
2. Vogel JP, Chawanpaiboon S, Watananirun K, et al. The global epidemiology of pre-eclampsia and eclampsia: a systematic review and meta-analysis. Lancet Glob Health. 2021;9(9):e1236–e1245. doi:10.1016/S2214-109X(21)00268-0
3. Romero R, Dey SK, Fisher SJ. Preterm labor: One syndrome, many causes. Science. 2022;377(6606):284–289. doi:10.1126/science.abq4074
4. Singh S, Kumari R, Jain S. Serum IL-6, TNF-α and CRP Levels in Women With Pre-Eclampsia and Their Relationship With Urinary Tract Infection. J Obstet Gynaecol Res. 2023;49(4):1256–1264. doi:10.1111/jog.15576
5. ElzenBono MJ, Leslie SW. Uncomplicated Urinary Tract Infections. 2025 Feb 21. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. PMID: 29261874.
6. Smaill FM, Vazquez JC. Antibiotics for asymptomatic bacteriuria in pregnancy. Cochrane Database Syst Rev. 2015 Aug 7;(8):CD000490. doi: 10.1002/14651858.CD000490.pub3. Update in: Cochrane Database Syst Rev. 2019 Nov 25;2019(11). doi: 10.1002/14651858.CD000490.pub4. PMID: 26252501.
7. Sheppard M, Ibiebele I, Nippita T, Morris J. Asymptomatic bacteriuria in pregnancy. Aust N Z J Obstet Gynaecol. 2023 Oct;63(5):696-701. doi: 10.1111/ajo.13693. Epub 2023 May 8. PMID: 37157162.