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Association of Urinary Tract Infection with Preeclampsia during Pregnancy

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ABSTRACT

Background: Urinary tract infections (UTIs) during pregnancy have a wide range of impacts on fetomaternal outcomes. **Objective:** To find association of UTIs with preeclampsia in pregnancy. **Study design:** Cohort study. **Place and duration of study:** Obstetrics and Gynecology Department, PAF Hospital, Islamabad. **Materials and Methods:** After obtaining approval from Institutional Ethical Committee, 140 women coming for routine antenatal checkup were divided into two groups (exposed or non-exposed) based on having UTI. The women were followed up to parturition and frequency of preeclampsia was noted down. The data was analysed by SPSS version 25. The relative risk (RR) was calculated for the exposed and non-exposed groups. **Results:** The mean age of the patients was 29.91 ± 5.98 years. The mean gestational age and BMI at time of recruitment were 28.92 ± 4.37 weeks and 24.08 ± 2.58 kg/m^2 respectively. Out of 140 patients, 39 (27.9%) developed preeclampsia. In the exposed group, 26 (37.1%) while in the unexposed group, 13 (18.6%) patient developed preeclampsia (p = 0.014). The RR was 2.00 (95% CI 1.123-3.563). The Odds ratio for UTI (exposed/unexposed) was 2.591 (95% CI 1.196-5.614). The binary logistic regression analysis showed that effect of confounder was not statistically significant (p = 0.077). **Conclusion:** UTIs independently increases preeclampsia risk in pregnancies beyond 20 weeks. Despite confounding variables, this association necessitate for routine UTI screening and early antibiotic treatment in antenatal care.

INTRODUCTION

Urinary tract infections (UTIs) are a significant clinical concern, representing one of the most common bacterial infections in women, particularly during pregnancy. Globally, UTIs account for a substantial proportion of healthcare visits and are implicated in severe complications, including maternal and neonatal morbidity. The physiological and anatomical changes that occur during pregnancy, such as urinary stasis, hormonal influences, and alterations in the immune system, increase susceptibility to both asymptomatic bacteriuria and symptomatic UTIs.[1, 2] These infections can escalate to severe outcomes if untreated, with potential risks to maternal and fetal health, including preterm labor, low birth weight, and perinatal mortality. [3] Concurrently, preeclampsia, a hypertensive disorder of pregnancy, which 0.2 to 9.2% of pregnancies, remains a leading cause of maternal and fetal complications. With its multifactorial etiology involving placental ischemia, systemic inflammation, and endothelial dysfunction, preeclampsia poses a critical challenge in obstetric care.[4]
The relationship between UTIs and preeclampsia is an area of considerable clinical interest yet remains controversial. While some studies have highlighted an association between maternal infections, including UTIs, and an increased risk of preeclampsia, others have yielded conflicting results. [5] Factors such as immune system dysregulation, systemic inflammation, and endothelial dysfunction, which are central to preeclampsia, may be exacerbated by UTIs. Despite extensive research, inconsistencies in prevalence estimates, study designs, and patient populations have hindered a definitive understanding of this association. [6]
Taghavi Zahedkalaei, A., et al. that UTI increases the risk of preeclampsia [OR=1.86, (95% Confidence: 2.235–1.608) (p<0.043). [4] Yaqub, U., et al. found that 40% and 17.5% patients developed preeclampsia with and without UTI exposure respectively (p value 0.036). [6]
Kaduma, J., et al. showed that among 393 pregnant women enrolled, 110 (28.0%), had significant bacteriuria and women with preeclampsia had 7.7 odds of having significant bacteriuria (p-value <0.001).[7] Radu, V. D., et al. found that there was no association of UTI and preeclampsia (aOR 2.07 with 95% CI 0.63-6.65, P value = 0.22). [8] These knowledge gaps underscore the need for region-specific studies to assess whether UTIs contribute to preeclampsia and how they might influence maternal and perinatal outcomes, particularly in populations with

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distinct socioeconomic, healthcare, and environmental factors.[9, 10]
The current study aimed to investigate the association between UTIs and preeclampsia during pregnancy in Pakistan, where both conditions significantly contribute to maternal and neonatal morbidity and mortality. Pakistan's high burden of maternal infections and hypertensive disorders of pregnancy necessitates targeted research to identify preventable risk factors and improve clinical outcomes.[3, 6] By exploring the association between UTIs and preeclampsia, this research seeks to provide evidence-based insights that can inform public health strategies, enhance prenatal care protocols, and ultimately reduce the adverse effects of these conditions on maternal and fetal health in this region.

METHODOLOGY

This cohort study was conducted from 1st of January 2025 to 30th of April 2025 at Obstetrics and Gynecology department of PAF Hospital, Islamabad. The Institutional Ethical approval was taken (Application no 241203, Dated 03 December 2024) before conducting this research. The trial was registered on clinicaltrials.gov (NCT). The sample size of A sample size of 140 patients (70 exposed, 70 non-exposed) is calculated using 5% level of significance, 80% power of test. The frequency of preeclampsia was taken as 40% in exposed group and 17.5% in non-exposed group.[6] Women attending outpatient department for routine antenatal checkup, with gestational age >20 weeks by LMP, and aged 18–35 years were included in the study. The women with history of diabetes mellitus, chronic hypertension, chronic liver/kidney/pulmonary diseases, urological surgery in the past 3 months, renal transplant, immunosuppression, coagulation disorders, or recent use of drugs causing proteinuria (NSAIDs, chemotherapeutics, ARBs, hydralazine) were excluded from the study. All patients were counselled regarding the research protocol, and informed written consent was obtained. They underwent clinical evaluation and relevant investigations. Pregnant women were instructed to collect a midstream urine sample (approximately 10 mL) in a sterile, wide-mouth container after washing their hands with water and cleaning the genital area using a normal saline-soaked swab. The samples were either sent to the laboratory within two hours or refrigerated at 4°C and delivered within 18 hours of collection. The urine samples were centrifuged and sedimented for routine urine examination. The UTI was labelled as having >5 pus cells/high power field (HPF). Patients were categorized as having UTI (exposed) or not having UTI (non-exposed) based on results. The selection process continued via non-probability consecutive sampling until both exposed and non-exposed groups had 70 women in each of them. All patients were followed until parturition. The frequency of preeclampsia was assessed per operational definitions (It will be defined as BP >140/90 mmHg on minimum two occasions after 20 weeks of pregnancy alongside presence of proteinuria (≥300 mg/day or at least 1+ dipstick testing or spot urine protein/creatinine ratio of ≥30 mg/mmol) by a consultant who remained blinded to the UTI exposure status. Management followed standard hospital protocols. All the data was collected on specially designed proforma.

Data were analysed using SPSS version 25 (Statistical Package for Social Sciences) for Microsoft Windows. Quantitative variables such as age, gestational age, and BMI were expressed as mean ± standard deviation (SD), while categorical variables like parity, UTI status, and preeclampsia occurrence were presented as frequencies and percentages. The relative risk (RR) or Odds ratio (OR) for preeclampsia development was calculated to compare the exposed (UTI-positive) and non-exposed (UTI-negative) groups. To account for potential confounding effects such as age, gestational age, parity and BMI, binary logistic regression analysis was performed. P-value ≤ 0.05 was considered statistically significant.

RESULTS

We had the data of 140 patients at the end of our study period. During follow up process, 13 patients lost follow up, so additional cases were recruited to get the final targeted number of patients, i.e., 70 in each group of 70 patients. The mean age of the patients was 29.91 ± 5.98 years. The mean gestational age and BMI at time of recruitment were 28.92 ± 4.37 weeks and 24.08 ± 2.58 kg/m^2 respectively. Out of 140 patients, 39 (27.9%) developed preeclampsia.
As given in Table 1, the exposed group, 26 (37.1%) while in the unexposed group, 13 (18.6%) patient developed preeclampsia (p = 0.014). The RR was 2.00 (95% CI 1.123-3.563). The Odds ratio for UTI (exposed/unexposed) was 2.591 (95% CI 1.196-5.614).
The binary logistic regression analysis was conducted to assess the association between UTI and the risk of preeclampsia, while adjusting for potential confounders including age, gestational age, BMI, and parity (Table 2). The model correctly classified 75.7% of the cases, with a higher accuracy for non-preeclampsia (99.0%) compared to preeclampsia cases (15.4%). Age showed a marginal association (p = 0.087), while gestational age, BMI, and parity were not significant predictors (p > 0.05). The overall model was not statistically significant (p = 0.077), suggesting that the predictors, as a group, did not improve the model fit significantly.

Table 1
Uti and Preeclampsia Risk

			Preeclampsia		Total	Stats
			Yes	No		
UTI	Yes	N	26	44	70	OR (odds ratio)
		%	37.1%	62.9%	100.0%	UTI (Yes/No)
	No	N	13	57	70	2.591
		%	18.6%	81.4%	100.0%	(95% CI 1.196-5.614)
Total		N	39	101	140	
		%	27.9%	72.1%	100.0%	P value 0.013

Table 2
UTI and Confounders on Risk of Preeclampsia

Variable	B	S.E.	Wald	P value	aOR	95% CI
UTI (Yes)	-0.997	0.402	6.163	0.013	0.369	0.168 – 0.811
Age (years)	-0.058	0.034	2.935	0.087	0.944	0.884 – 1.008
Gestational Age (weeks)	-0.010	0.045	0.046	0.831	0.990	0.907 – 1.082
BMI	-0.030	0.077	0.152	0.697	0.970	0.835 – 1.128
Parity	0.118	0.116	1.039	0.308	1.125	0.897 – 1.411
Constant	3.947	2.606	2.293	0.130	51.776	

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DISCUSSION

Preeclampsia is a multisystem hypertensive disorder during gestation that remains a leading cause of maternal and perinatal morbidity and mortality worldwide. [11] The literature shows that preeclampsia complicates 2-8% of pregnancies and contributes significantly to adverse outcomes, including preterm birth, intrauterine growth restriction, and maternal organ dysfunction. [12] Despite extensive research, the exact etiology of preeclampsia remains elusive, though it is widely accepted that placental dysfunction, endothelial damage, and systemic inflammation play key roles in the pathophysiology of this condition and its adverse sequel. [13, 14]

Among the various risk factors investigated, UTIs have emerged as a potential contributor to preeclampsia development and progression. UTIs are the most common bacterial infections encountered in pregnancy, affecting up to 10-20% cases, with higher prevalence in low-resource settings. [1] The association between UTIs and preeclampsia has been explored in multiple studies, yet the nature of this relationship—whether causal, confounded, or merely correlational—remains debated among many authors. [15]

Our study found that pregnant women with UTIs had a two-fold increased risk of developing preeclampsia (RR: 2.00, 95% CI: 1.123–3.563), with an adjusted odds ratio (aOR) of 0.369 (95% CI: 0.168–0.811) after controlling for confounders like age, gestational age, BMI and parity. The results in our study align with multiple observational studies and meta-analyses suggesting that UTIs increase the risk of preeclampsia:

Conde-Agudelo et al. conducted a systematic review and meta-analysis of 49 studies, finding that UTIs were associated with a 57% increased risk of preeclampsia (pooled OR: 1.57, 95% CI: 1.45–1.70). [16] Similarly, Yan et al. found in another meta-analysis of 19 studies and reported that women with UTI had 31% higher risk (OR: 1.31, 95% CI: 1.22–1.40). In a case control study by Kaduma et al. in Tanzanian, found that women with preeclampsia had 7.7 times higher odds of significant bacteriuria OR: 7.7, 95% CI: 4.11–14.49). Our study focused on the women with >20 weeks of gestation but UTI in any trimester can increase the risk of preeclampsia as Easter et al. demonstrated that UTIs, particularly in the third trimester, tripled the risk of preeclampsia (aOR: 3.2, 95% CI: 2.0–5.1). [17] These studies collectively suggest that UTIs either trigger or exacerbate preeclampsia, possibly through systemic inflammation or immune dysregulation.

As we find the literature regarding this association some studies with contradictory findings are encountered. Karmon & Sheiner argue that the relationship may be confounded by shared risk factors (e.g., poor socioeconomic status, chronic hypertension, or pre-existing renal dysfunction). [15] Moreover, some studies did not adjust for key variables such as obesity, diabetes, or prior UTIs, which could independently influence the risk of preeclampsia. [10] Our study attempted to control for confounders (age, BMI, parity, gestational age), but the overall logistic regression model showed no statistically significant associations ($p = 0.077$). This suggests that while UTIs show an independent association, other confounders like genetic predisposition, nutritional status, or environmental exposure may also play a role. [5]

The UTIs and risk of preeclampsia has many underlying biological mechanisms which may share the same inflammatory pathways. The systemic inflammation and endothelial dysfunction have been caused by preeclampsia and similar mechanisms are shared by UTIs particularly, pyelonephritis. The increased pro-inflammatory cytokines like (IL-6, TNF-α, CRP) and oxidative stress due to bacterial endotoxins (e.g., lipopolysaccharides from E. coli) is also common in both conditions. [17] The complement system activation may contribute to placental ischemia. These mechanisms may synergize with placental dysfunction and thus may lead to clinical manifestations of preeclampsia like hypertension, proteinuria, and systemic organ involvement. [18]

Some researchers propose that subclinical renal damage from prior UTIs like childhood pyelonephritis may predispose women to preeclampsia in adult age. This hypothesis is supported to some extent by histopathological similarities between focal segmental glomerulosclerosis (seen in chronic UTIs) and glomerular endotheliosis (a hallmark of preeclampsia). [19] Ghouri et al. found that there is emerging evidence that alterations in the urinary or vaginal microbiome may influence preeclampsia risk. E. coli and Klebsiella, which are uropathogens may disrupt immune tolerance, promoting a pro-inflammatory state that exacerbates placental dysfunction. [2]

The various studies included other potential confounders which may affect the relationship between UTIs and the risk of preeclampsia. Our study was limited to only age, gestational age, BMI and parity as confounders. Stitterich et al. showed that low socioeconomic status is linked to both UTIs (due to poor hygiene, limited healthcare access) and preeclampsia. [5] The obesity and diabetes also among independent risk factors for the risk of preeclampsia. [10] Some women with family history may confound the association of UTI and risk of preeclampsia which suggests genetic predisposition may play significant role. [5, 10]

Our study had a small sample size of 140 patients which limits generalizability. Moreover, non-categorization of UTI between asymptomatic versus symptomatic, which may have different impacts. The selection bias may exist potentially as this study was single-centered. The long-term follow-up was not planned in our objectives, which would provide more insight into the persistent renal effects.

Given the strong association between UTI and risk of preeclampsia, universal midstream urine culture screening should be implemented, particularly in high-risk populations. [18] Early antibiotics should be the focus during prompt treatment of asymptomatic bacteriuria, which may reduce preeclampsia risk. [20] The improvement in hydration, perineal hygiene, and prenatal care adherence by patient education and awareness can reduce UTI incidence. [1]

For further future research directions should focus on large multicenter cohort studies with longitudinal UTI monitoring. The randomized controlled trials would

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assess whether UTI treatment reduces preeclampsia incidence. The role of urine culture to identify high risk microbes should be focused on. Our study supports the hypothesis that UTIs are an independent risk factor for preeclampsia in women with >20 weeks of gestation, likely through inflammatory and endothelial injury pathways. While various confounding factors exist, the evidence is strong enough to justify enhanced UTI screening and prompt treatment protocols in antenatal care. Future research should focus on targeted interventions to mitigate this risk.

CONCLUSION

Our findings confirm that UTIs independently increase preeclampsia risk in pregnancies beyond 20 weeks. Despite confounding variables, this association necessitate for routine UTI screening and early antibiotic treatment in antenatal care. Further research should explore targeted therapeutic strategies to reduce preeclampsia incidence in high-risk women.

Authors' Contribution

WF, NS: Conception and design, Collection and assembly of data, and guarantor
NS, ST: Critical revision for important intellectual content, final approval
WF, IKM, AH, AN: Analysis and interpretation of data, Statistical expertise.

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