

The Predictive Value of Inflammatory Indices For Urine Culture Positivity In Pregnant Women Presenting With Lower Urinary Tract Symptoms

Ezgi Basaran^{1*}, Ulku Gurbuz Ozbebek², Ayse Gulcin Bastemur¹, Atakan Tanacan¹, Dilek Sahin¹

¹Department of Obstetrics and Gynecology, Division of Perinatology, Turkish Ministry of Health Ankara Bilkent City Hospital, Ankara, Türkiye

²Department of Obstetrics and Gynecology, Turkish Ministry of Health Ankara Bilkent City Hospital, Ankara, Türkiye

ABSTRACT

Urinary tract infection is one of the most common bacterial infections during pregnancy. However, not every pregnant woman presenting with lower urinary tract symptoms (LUTS) necessarily has an actual infection. Since urine culture, the gold standard for diagnosis, takes time to yield results, there is a need for rapid and practical diagnostic tools. This study aims to evaluate the effectiveness of systemic inflammatory indices in predicting urine culture positivity.

Pregnant women presenting with LUTS were retrospectively evaluated. A total of 106 patients were included, with 53 positive and 53 negative urine cultures. Complete blood count parameters and C-reactive protein (CRP) levels at admission were analyzed. Inflammatory indices—including the systemic immune-inflammation index (SII), systemic inflammation response index (SIRI), neutrophil-to-lymphocyte ratio (NLR), and aggregate systemic inflammation index (AISII)—were calculated and compared between the groups. Their predictive value for culture positivity was assessed.

Patients with positive cultures had significantly longer hospital stays ($p = 0.015$), higher rates of preterm birth ($p = 0.020$), and lower neonatal birth weight ($p = 0.015$). WBC, neutrophils, CRP, and all inflammatory indices were significantly higher in the culture-positive group (all $p < 0.001$). ROC analysis identified CRP as the most effective marker (AUC = 0.770; sensitivity: 76%, specificity: 70%), while SIRI was the most predictive inflammatory index (AUC = 0.742; sensitivity: 70%, specificity: 68%).

Inflammatory indices are useful in predicting urine culture positivity in pregnant women with LUTS. The combined use of CRP and SIRI with WBC and neutrophil counts may enhance diagnostic efficiency.

Keywords: pregnancy, urinary tract infections, lower urinary tract symptoms, inflammatory indices, biomarkers

Introduction

Although lower urinary tract symptoms (LUTS) are commonly observed during pregnancy, they do not always indicate the presence of an actual infection. (1) Complaints such as dysuria, frequent urination, and lower abdominal pain may occur in pregnant women even in the absence of infection, due to anatomical and physiological changes. (2) Hormonal changes, mechanical pressure, and physiological changes in the urinary system during pregnancy increase the risk of developing urinary tract infections (UTI). (3,4) In addition, UTI is the most common bacterial infection during pregnancy and is associated with significant obstetric and neonatal complications. (5) In a systematic review, the global prevalence of UTI in

pregnancy was reported as 20%; however, this rate appears to decrease as the study year progresses. (6) In a more recent prospective study, the incidence of UTI in low-risk pregnant women was reported as 9.4%. (7) The occurrence of a UTI can contribute to the development of adverse clinical outcomes like preterm birth and low birth weight. (7,8) It may progress to serious maternal complications, including pyelonephritis, sepsis, and acute respiratory distress syndrome (ARDS). (4)

For these reasons, accurately distinguishing LUTS in pregnant women is of great importance in avoiding unnecessary antibiotic use and hospital admissions. Although urine culture remains the gold standard for diagnosis, the time required for results hinders timely

*Corresponding Author: Ezgi Basaran, Department of Obstetrics and Gynecology, Division of Perinatology, Turkish Ministry of Health Ankara Bilkent City Hospital, Ankara, Türkiye

E-mail: ezgi.basrn@gmail.com, Phone: +90505 893 5424

ORCID ID: Ezgi Basaran: 0000-0002-5062-3316, Ulku Gurbuz Ozbebek: 0000-0003-1416-4850, Ayse Gulcin Bastemur: 0000-0001-8362-7324, Atakan Tanacan: 0000-0001-8209-8248, Dilek Sahin: 0000-0001-8567-9048

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clinical decision-making. In recent years, hemogram-based inflammatory indices, including the neutrophil-to-lymphocyte ratio (NLR), systemic immune-inflammation index (SII), systemic inflammatory response index (SIRI), and aggregate systemic inflammation index (AISI) have been used to predict disease severity and prognosis in various clinical settings. (9-13) Studies conducted in pediatric populations have demonstrated that these indices are effective in predicting febrile UTI, acute pyelonephritis, and severe bacterial infections (14-16). The use of inflammatory indices in the differential diagnosis of UTI during pregnancy may contribute to the rapid and accurate identification of patients requiring treatment. The objective of the present research was to determine whether inflammatory indices can effectively predict urine culture positivity in pregnant women presenting with LUTS.

Materials and Methods

This retrospective study was conducted among pregnant women who presented with symptoms of urinary tract infection to our perinatology clinic between January 2020 and April 2023. The study was approved by the Ethics Committee of Ankara Bilkent City Hospital (Approval No: E2-23-3803) and was carried out in compliance with the principles outlined in the Declaration of Helsinki. Written informed consent was obtained from all participants prior to inclusion. Pregnant women with additional systemic diseases, those diagnosed with pyelonephritis, patients without urine culture results and those with incomplete laboratory data were excluded from the study. A total of 106 patients were included in the study, comprising 53 with negative urine cultures (Group 1) and 53 with positive urine cultures (Group 2). Sociodemographic characteristics, obstetric history, clinical findings, obstetric outcomes, and laboratory values at admission, including hemogram, C-reactive protein (CRP), spot urine test, and urine culture results were recorded. The calculation of inflammatory indices was based on the following formulas:

- **NLR** = Neutrophil count / Lymphocyte count
- **SII** = (Neutrophil $\times$ Platelet) / Lymphocyte
- **SIRI** = (Neutrophil $\times$ Monocyte) / Lymphocyte
- **AISI** = (Neutrophil $\times$ Platelet $\times$ Monocyte) / Lymphocyte

Statistical analyses were performed using SPSS version 26 (IBM Corp., Chicago, IL, USA). The Kolmogorov-Smirnov test was used to assess the normality of distribution. Continuous variables were expressed as medians (minimum-maximum) and

compared between groups using the Mann-Whitney U test. Categorical variables were presented as counts and percentages, and group comparisons were made using the chi-square test.

Univariate analysis was conducted for WBC, neutrophils, CRP, NLR, SII, SIRI, and AISI to assess their predictive value for urine culture positivity. Receiver operating characteristic (ROC) curve analysis was subsequently conducted to identify the optimal cut-off values. The Youden index was used to identify the most appropriate thresholds. Statistical significance was defined as a p -value < 0.05 .

Results

The study population consisted of 106 patients, including 53 with negative urine cultures and 53 with positive urine cultures. No significant differences were observed between the groups with respect to maternal age, gestational age at admission, gestational age at delivery, 1st and 5th minute Apgar scores, or need for neonatal intensive care. Although the rate of composite adverse perinatal outcomes was higher in the culture-positive group (Group 1: 9.4% vs Group 2: 17%), the difference did not reach statistical significance ($p = 0.251$). By contrast, the culture-positive group had significantly longer hospital stay ($p = 0.015$), higher incidence of preterm birth ($p = 0.020$), and lower neonatal birth weight ($p = 0.015$). The clinical characteristics and obstetric outcomes are summarized in Table 1.

The frequencies of flank pain, dysuria, urinary frequency, and ultrasonographically detected hydronephrosis were similar between the groups. In spot urine analysis, however, leukocyte esterase and nitrite positivity were significantly more common in the culture-positive group ($p = 0.007$ and $p < 0.001$, respectively). WBC and neutrophil counts, CRP levels, and all calculated inflammatory indices (NLR, SII, SIRI, AISI) were significantly higher in the culture-positive group (all $p < 0.001$). A comparison of symptoms, ultrasonographic findings, laboratory parameters, and inflammatory indices is presented in Table 2.

In univariate logistic regression analysis, all parameters were effective in predicting culture positivity; WBC and neutrophil counts showed the strongest associations (OR = 1.36 and 1.35, respectively; 95% CI ≈ 1.16 –1.60; $p < 0.001$). Although CRP exhibited a lower effect in the univariate model (OR = 1.02; 95% CI 1.005–1.032; $p = 0.006$), it yielded the highest discriminative power in ROC analysis (AUC = 0.770; sensitivity 76%, specificity 70%). Among composite indices, SIRI was

Table 1: Clinical and Obstetric Characteristics of Pregnant Women with Lower Urinary Tract Symptoms by Urine Culture Results

	Culture Negative (n=53)	Culture Positive (n=53)	P value
Age, years	26 (17–40)	25.4 (18–41)	0.443
GA at admission, weeks	28 (14–39)	28 (12–39)	0.604
Total hospital stay, days	3 (0–13)	5 (0–16)	0.015
Dysuria	28/53	31/53	0.520
Urinary frequency	22/53	26/53	0.480
Flank pain	16/53 (30.2%)	17/53 (32.1%)	0.834
Right Hydronephrosis			0.094
None	25/53 (47.2%)	28/53 (52.8%)	
Grade 1	24/53 (45.3%)	15/53 (28.3%)	
Grade 2-3	3/53(5.7%)	10/53 (18.9%)	
Left Hydronephrosis			0.495
None	40/53 (75.5%)	44/53 (83.0%)	
Grade 1	11/53 (20.8%)	9/53 (17.0%)	
Grade 2-3	2/53 (3.8%)	0/53 (0%)	
GA at birth (weeks)	38 (30–41)	38 (31–41)	0.078
Birth weight (g)	3260 (1380–3900)	3020 (1660–3830)	0.015
1st minute Apgar score	7 (6–9)	7 (4–9)	0.981
5th minute Apgar score	9 (7–10)	9 (6–10)	0.443
Preterm birth	7/53 (13.2%)	17/53 (32.1%)	0.020
CAPO	5/53 (9.4%)	9/53 (17.0%)	0.251
NICU admission	8/53 (15.1%)	9/53 (17.0%)	0.791

Data presented as median (min-max) or n (%). Statistically significant at $p < 0.05$

GA: gestational age, CAPO: composite adverse perinatal outcome, NICU: neonatal intensive care unit

Table 2: Laboratory Findings of Patients with Negative and Positive Urine Culture Results

	Culture Negative (n=53)	Culture Positive (n=53)	P value
Leukocyte esterase			0.007
Negative	9/53 (17.0%)	3/53 (5.7%)	
1+	14/53 (26.4%)	4/53 (7.5%)	
2+	12/53 (22.6%)	17/53 (32.1%)	
3+	18/53 (34.0%)	29/53 (54.7%)	
Nitrite			<0.001
Negative	52/53 (98.1%)	30/53 (56.6%)	
Positive	1/53 (1.9%)	23/53 (43.4%)	
WBC ($10^9/L$)	9.90 (5.85-16.41)	12.20 (7.58-41.00)	<0.001
Neutrophil ($10^9/L$)	7.25 (3.86-14.57)	10.06 (5.69-35.46)	<0.001
Monocyte ($10^9/L$)	0.46 (0.140-7.76)	0.56 (110-2.60)	<0.001
Lymphocyte ($10^9/L$)	1.60 (0.20-2.70)	1.33 (0.26-3.04)	0.028
Platelet ($10^9/L$)	233 (135-583)	236 (114-601)	0.422
CRP (mg/L)	3 (0-136)	15 (1-270)	<0.001
NLR	4.6 (2.3-35.3)	8.2 (1.9-35.3)	<0.001
SII	1092.5 (460.7-8280)	1858.2 (517.8-21300)	<0.001
SIRI	2.1 (0.9-32.1)	4.5 (0.9-40.6)	<0.001
AISI	575.7 (180-7600)	998 (254-11900)	<0.001

Data presented as median (min-max) or n (%). Statistically significant at $p < 0.05$

AISI, aggregated index of systemic inflammation; NLR, neutrophil-to-lymphocyte ratio; SII, systemic inflammation index; SIRI, systemic inflammatory response index, WBC: white blood cell

Table 3: Univariate Logistic Regression of Laboratory Parameters and Inflammatory Indices for the Prediction of Urine Culture Positivity

	OR	P value	95 %CI
WBC ($10^9/L$)	1.36	<0.001	1.159-1.584
Neutrophil ($10^9/L$)	1.37	<0.001	1.166-1.606
CRP (mg/L)	1.02	0.006	1.005-1.032
NLR	1.14	0.004	1.043-1.248
SII	1.00	0.005	1.000-1.001
SIRI	1.13	0.019	1.021-1.255
AISI	1.00	0.018	1.000-1.001

Statistically significant at $p < 0.05$

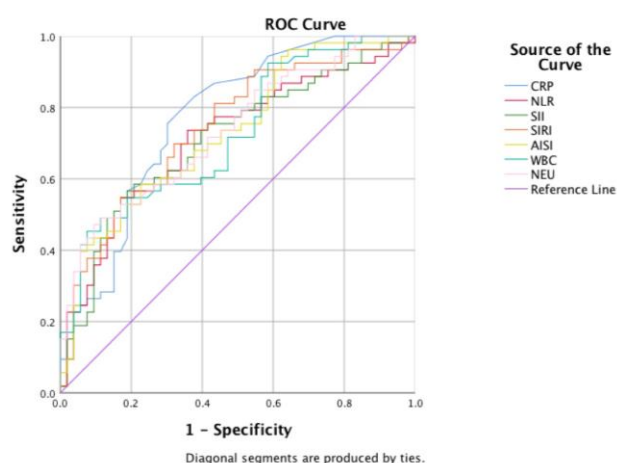
OR: odds ratio, CI: confidence interval, AISI: aggregated index of systemic inflammation, CRP: C-reactive protein, NLR: neutrophil-to-lymphocyte ratio, SII: systemic inflammation index, SIRI: systemic inflammatory response index, WBC: white blood cell

Table 4: ROC Curve Analysis of Laboratory Parameters and Inflammatory Indices for the Prediction of Urine Culture Positivity

	Cut-off	AUC	95%CI	P value	Sensitivity (%)	Specificity (%)
WBC ($10^9/L$)	9.91	0.725	0.63-0.82	<0.001	72	53
Neutrophil ($10^9/L$)	7.67	0.735	0.64-0.83	<0.001	72	59
CRP (mg/L)	5.5	0.770	0.68-0.86	<0.001	76	70
NLR	5.3	0.715	0.62-0.81	<0.001	70	66
SII	1225.3	0.712	0.61-0.81	<0.001	70	63
SIRI	2.96	0.742	0.66-0.84	<0.001	70	68
AISI	604	0.730	0.64-0.82	<0.001	70	59

Statistically significant at $p < 0.05$

AUC: area under the curve, CI: confidence interval, AISI, aggregate index of systemic inflammation; CRP: C reactive protein, NLR: neutrophil-to-lymphocyte ratio, SII: systemic inflammation index, SIRI: systemic inflammatory response index, WBC: white blood cell

**Fig. 1.** ROC curves of the laboratory parameters and inflammatory indices for the prediction of urine culture positivity

the most effective predictor among the inflammatory indices (AUC = 0.742; sensitivity 70%,

specificity 68%). WBC, NLR, SII, and AISI were also predictive, but with lower AUC values. Optimal cut-off values identified by ROC analysis were 5.5 mg/L for CRP, and 2.96 for SIRI. Univariate analysis results are detailed in Table 3, ROC analysis in Table 4, and the ROC curve is illustrated in Figure 1.

Discussion

During pregnancy, urinary tract infections are prevalent and may result in serious adverse outcomes for both the mother and the fetus. In addition to neonatal outcomes such as preterm birth and low birth weight, UTIs can progress to severe maternal conditions including pyelonephritis, sepsis and acute respiratory distress syndrome (ARDS). (4,7,8)

While diagnostic parameters such as leukocyte esterase and nitrite in urine analysis play a significant

role in the general population, leukocyte esterase positivity is frequently observed in pregnant women due to vaginal contamination, resulting in reduced specificity (4). Nitrite is a highly specific marker, but it is not present in all bacterial infections. (4) The long turnaround time for urine culture, which is the gold standard for diagnosis, and the limited ability of conventional laboratory parameters to distinguish actual infection highlight the need for new, rapid, and accurate diagnostic tools. Additionally, the rising concerns over cost-effectiveness, increasing antibiotic resistance, and potential fetal risks necessitate avoidance of overtreatment (1).

Traditionally, systemic infection has been assessed using parameters such as WBC, neutrophil count, and CRP. In recent years, new inflammatory indices combining hemogram parameters such as NLR, SII, SIRI, and AISI have been defined.

In our study, we evaluated the relationship between inflammatory indices and urine culture positivity in pregnant women presenting with LUTS. Our findings revealed that all inflammatory indices were significantly higher in the culture-positive group, and that each marker had predictive value, with CRP and SIRI emerging as the most effective parameters for diagnosis. While WBC and neutrophil counts were the strongest predictors in univariate analysis, CRP demonstrated the highest discriminative performance in ROC analysis, with 76% sensitivity and 70% specificity. SIRI, as the most effective inflammatory index, also proved to be a potentially valuable tool in clinical practice.

CRP is a well-established acute-phase reactant and has been used for a long time as a systemic marker of inflammation (17). It has been shown to reduce unnecessary antibiotic use in upper respiratory infections, to correlate with clinical deterioration in COVID-19 patients, and to serve as a prognostic indicator in cardiovascular and rheumatologic diseases (18-21). Consistent with these findings, our study identified CRP as the most reliable marker for predicting culture positivity.

In a 2023 pediatric study by Elgormus et al., NLR, SII, and CRP were found to be significant predictors of culture positivity, with CRP demonstrating the highest specificity (16). Another pediatric study reported that CRP and NLR were the most effective markers for predicting acute pyelonephritis and NLR for vesicoureteral reflux (15). Aligning with this literature, our results confirm the predictive value of all inflammatory markers, with CRP being the most reliable.

Several studies conducted on pregnant populations have also highlighted the diagnostic and prognostic

value of inflammatory indices in various clinical conditions. For instance, SII has been found to have diagnostic value in distinguishing between ulcerative colitis and healthy pregnancies (22). It has also been suggested as a potential marker for predicting intrahepatic cholestasis of pregnancy (23). In patients with hyperemesis gravidarum, all inflammatory indices were associated with disease severity, with SIRI having the highest diagnostic performance (24). Moreover, SII and SIRI have been reported as predictive tools in cases of recurrent pregnancy loss (25). AISI, a relatively newer index, has shown prognostic utility in infectious conditions such as COVID-19 and chorioamnionitis (26-28).

While our findings are promising, this study has several limitations. First, its retrospective and single-center design may limit the generalizability of the results. Second, the relatively small sample size may have reduced the statistical power and restricted subgroup analyses. Finally, patients with adverse perinatal outcomes represented only a small proportion of the study cohort. Future multicenter studies with larger sample sizes are warranted to validate the utility of inflammatory indices as reliable predictors of culture positivity.

Our results, consistent with existing literature, suggest that inflammatory indices may be valuable tools in predicting culture positivity in pregnant women presenting with LUTS. In conclusion, WBC and neutrophil counts, which are easily accessible in routine practice, offer practical advantages but are limited by their low specificity. Although NLR, SII, and AISI also demonstrated predictive value for culture positivity, their performance was inferior to that of CRP and SIRI. In our study, $\text{CRP} \geq 5.5 \text{ mg/L}$ and $\text{SIRI} \geq 2.96$ were found to offer the most balanced performance in identifying culture-positive patients. The combined use of CRP and SIRI with WBC and neutrophil counts may enhance diagnostic accuracy in the differential diagnosis of UTI during pregnancy and contribute to reducing unnecessary treatment and hospitalization.

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