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ORIGINAL RESEARCH

Pathogen Resistance and Biomarker-Based Diagnosis of Postoperative Urinary Tract Infections in Kidney Stone Patients

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Background: Urinary tract infections (UTIs) are postoperative complications following kidney stone surgery, especially in regions with increasing antimicrobial resistance (AMR). In China, high resistance rates of uropathogens to commonly used antibiotics pose major challenges for effective treatment. This study aimed to investigate the pathogen spectrum, antimicrobial resistance patterns, and diagnostic utility of inflammatory biomarkers in postoperative UTIs among patients with kidney stones.

Methods: This prospective observational study was conducted at a tertiary hospital in China, enrolling 130 patients who underwent kidney stone surgery between February 2021 and December 2024. Based on postoperative infection status, patients were classified into UTI (n=41) and Non-UTI groups (n=89). Blood samples were collected to assess inflammatory markers, including high-sensitivity C-reactive protein (hs-CRP), heparin-binding protein (HBP), neutrophil gelatinase-associated lipocalin (NGAL), and adiponectin (ADPN). Midstream urine samples from UTI patients were cultured for pathogen identification and antimicrobial susceptibility testing. Pearson correlation, receiver operating characteristic (ROC) analysis, and multivariate logistic regression were performed.

Results: A total of 67 isolates were identified, mainly Gram-negative bacteria [59.70%; *Escherichia coli (E. coli), Pseudomonas aeruginosa (P. aeruginosa), Klebsiella pneumoniae (K. pneumoniae)*], Gram-positive bacteria (32.84%), and fungi (7.46%). Most Gram-negative isolates showed >85% resistance to AMP, while remaining sensitive to imipenem. UTI patients had higher white blood cell counts, hs-CRP, HBP, NGAL, and lower ADPN levels (all P<0.001). Among biomarkers, HBP and ADPN showed high diagnostic value (AUC=0.8193 and 0.8719), and their combination with hs-CRP and NGAL achieved excellent accuracy (AUC=0.9496). HBP and NGAL were independent risk factors, while ADPN (OR=0.379, P<0.001) was protective.

Conclusion: Postoperative UTIs in kidney stone patients are dominated by resistant Gram-negative bacteria. Combined biomarker detection (hs-CRP HBP, NGAL, ADPN) provides a reliable model for early infection diagnosis and risk stratification, supporting clinical decision-making.

Keywords: urinary tract infection, kidney stones, antimicrobial resistance, inflammatory biomarkers, adiponectin, HBP, diagnostic model

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Introduction

Kidney stones represent a significant component of the global burden of urological diseases, with a remarkable epidemiological shift observed over the past two decades.[1] According to the World Health Organization, the prevalence of nephrolithiasis in adults has reached 7–13% in developed countries. Meanwhile, in developing regions, the incidence continues to rise by more than 5% annually, largely attributed to the westernized dietary habits and the increasing prevalence of metabolic syndrome.[2] Awedew et al analyzed data from the GBD 2000–2021 study and found that the global number of deaths related to urolithiasis increased by approximately 60.3% over the 21-year period, with a significant rise in the age-standardized death rate (ASDR).[3] In addition, Qian et al reported that from 1990 to 2019, the total number of deaths attributable to urolithiasis rose from approximately 11,338 to 13,227 per year. Although the

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ASDR showed a declining trend, the absolute number of deaths continued to increase.[4] A study from England and Wales indicated that urolithiasis-related deaths accounted for 0.1% of all deaths among the elderly population, with a clear year-on-year increase.[5] Collectively, international estimates suggest that more than 300,000 deaths occur globally each year due to stone-related complications such as sepsis and acute kidney injury (AKI). This burden is particularly pronounced in low- and middle-income countries, where limited healthcare resources contribute to higher mortality and misdiagnosis rates.

The pathogenesis of kidney stone formation is multifaceted, involving metabolic disturbances such as calcium dysregulation, uric acid homeostasis imbalance, and oxalate overload, as well as urinary tract anatomical abnormalities (eg, ureteropelvic junction obstruction) that disrupt urine flow and promote crystal deposition.[6,7] In recent years, minimally invasive surgical techniques such as ultrasound-guided percutaneous nephrolithotomy (PCNL) and digital flexible ureteroscopy with holmium laser lithotripsy (RIRS) have reduced surgical trauma. However, postoperative complications remain a major clinical challenge.[8] Among these complications, urinary tract infection (UTI) is one of the most frequently encountered, with an incidence of up to 35% in complex stone cases. Alarmingly, approximately 12% of postoperative UTI cases may progress to sepsis if not promptly managed.[9–11] The occurrence of postoperative UTI is not only associated with urinary obstruction and mucosal injury caused by calculi, but also influenced by the virulence of uropathogens, such as toxin secretion, biofilm formation, and adhesin expression and multiple drug resistance mechanisms.[12] In recent years, the prevalence of drug-resistant uropathogens has shown an upward trend, particularly extended-spectrum beta-lactamase-producing *Escherichia coli (E. coli)* and *Klebsiella pneumoniae* *(K. pneumoniae)*, which pose significant challenges to empirical antimicrobial therapy for postoperative UTIs.[13] The multidrug resistance of these pathogens not only complicates treatment strategies but also increases the risk of urosepsis, prolongs hospitalization, and significantly elevates healthcare costs. High-risk populations, such as patients with kidney stones complicated by diabetes, immunosuppression, or long-term catheterization, are more prone to persistent infections, poor treatment outcomes, and even severe complications like sepsis.[14] In China, with the continuous rise in the prevalence of urolithiasis, the clinical burden of managing postoperative infectious complications and drug-resistant pathogens has been increasing annually.[15] However, precise diagnostic tools and risk stratification systems for postoperative UTI in this patient population remain inadequate, and reliable biomarkers for early-stage infection detection are still lacking.

Recent studies have highlighted the promise of multidimensional biomarkers for early diagnosis and risk assessment of infectious diseases. High-sensitivity C-reactive protein (hs-CRP) is a well-established inflammatory marker; however, its ability to distinguish between infection and postoperative non-infectious stress responses (eg, surgical trauma and tissue repair) is limited.[16] Heparin-binding protein (HBP), a specific product of neutrophil (NEU) activation, has been shown to exhibit high sensitivity and specificity in the early diagnosis of sepsis. Nevertheless, its application in UTI remains underexplored.[17] Neutrophil gelatinase-associated lipocalin (NGAL), a small secretory glycoprotein, has been extensively investigated for its role in the early detection, treatment, and prognostic evaluation of AKI.[18] Additionally, NGAL has demonstrated clinical utility in diagnosing, monitoring, and managing chronic kidney disease and cardiorenal syndrome.[19] However, its specific diagnostic value in post-nephrolithiasis UTI has not yet been systematically assessed. Adiponectin (ADPN), a key anti-inflammatory metabolic regulator, has been implicated in infection pathophysiology, with decreasing levels potentially associated with both the occurrence and severity of infections.[20] Despite these insights, the independent diagnostic efficacy of these biomarkers in postoperative UTI following kidney stone surgery remains insufficiently validated, and the potential advantages of their combined application warrant further investigation.

Therefore, the present study aims to characterize the distribution and antimicrobial resistance patterns of pathogens responsible for postoperative UTI following kidney stone surgery, providing a reference for empirical antimicrobial treatment. Additionally, we seek to evaluate the diagnostic value of hs-CRP, HBP, NGAL, and ADPN in postoperative UTI and to develop a predictive model integrating multiple biomarkers. This model is expected to enable early warning and risk stratification of postoperative infections. The findings of this study may offer new insights and practical guidance for optimizing perioperative management strategies and reducing infection-related complications.

Materials and Methods

General Information

The sample size was calculated by referencing the difference in white blood cell (WBC) counts reported as an outcome measure in a previous study,[21] which yielded an effect size (Cohen's d) of 0.54. Based on this effect size, the required sample size for an independent samples *t*-test was estimated using G*Power version 3.1.9.7 software, with a significance level (α) of 0.05 (two-tailed) and a power (1- β) of 0.80. The calculation indicated a total sample size of 110 subjects. Accounting for an anticipated 10% dropout or missing data rate, the final planned enrollment was set at 130 patients to ensure adequate statistical power for the study.

This study is a prospective observational study, which included 130 patients with renal stones who underwent PCNL at our hospital between February 2021 and December 2024. Based on the presence of postoperative UTI, patients were categorized into the UTI group (n=41) and the Non-UTI group (n=89). The mean age of patients in the UTI group was 52.76±8.49 years, comprising 24 males and 17 females, whereas the Non-UTI group had a mean age of 53.03±7.12 years, including 43 males and 46 females. No statistically significant differences were observed in baseline characteristics between the two groups (P>0.05).

This study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Suzhou Hospital of Integrated Traditional Chinese and Western Medicine (No. 2025-008). Written informed consent was obtained from all participants.

Inclusion criteria: Age ≥18 years; Diagnosis of urinary calculi confirmed by CT, X-ray, or ultrasound; Complete clinical data available.

Exclusion criteria: Presence of active UTI or other infections prior to surgery; Coexisting urological disorders (eg, bladder cancer, neurogenic bladder); Prolonged use of immunosuppressants or antibiotics (>2 weeks).

Methods

Clinical Symptom Collection

Clinical symptoms occurring at the time of postoperative UTI onset, including urinary frequency (defined as increased urination, ie, pollakiuria), urgency, dysuria, pyuria, and fever, were collected from electronic medical records.

Surgery and Postoperative Management

All patients underwent standard PCNL under epidural anesthesia, with intraoperative placement of a double-J stent and drainage tube. Postoperatively, all patients received routine antibiotic prophylaxis (eg, cefuroxime or levofloxacin [LVX]) and, when necessary, nonsteroidal anti-inflammatory drugs, typically for a duration of 3–5 days. The selection and administration of antimicrobial agents followed the Chinese Clinical Application Guidelines for Antimicrobial Drugs (latest edition) and the hospital's antimicrobial stewardship protocols.[22] All regimens were reviewed and formulated by infectious disease specialists in collaboration with clinical pharmacists to ensure the rationality of the treatment and its alignment with the local resistance profile. Postoperative infection was diagnosed based on symptoms such as fever, urinary frequency and urgency, lower abdominal pain, and elevated white blood cell counts. To clarify the type of postoperative infection, all infected patients presented with bladder irritation symptoms without evidence of hydronephrosis or renal parenchymal changes, and were therefore classified as having lower urinary tract infections.

Sample Collection and Testing

Venous blood (2 mL) was collected on postoperative day 2, which was analyzed using an automated hematology analyzer (BC-5000, Mindray Bio-Medical Electronics Co., Ltd., Shenzhen, China) to determine WBC count, neutrophil-to-lymphocyte ratio (NLR), and NEU count. Additionally, 5 mL of venous blood was drawn and allowed to stand at room temperature for 15 minutes before being centrifuged at 4°C for 10 minutes using a low-speed refrigerated centrifuge (KDC-2046, Zhongjia Scientific Instrument Co., Ltd., China) to separate the serum. The expression levels of hs-CRP, HBP, NGAL, and ADPN were measured using an automated biochemical analyzer (008AS, Hitachi High-Technologies Corporation, Japan) with corresponding commercial assay kits: hs-CRP (Abcam, ab99995, UK), HBP

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(Cusabio, CSB-E15091h, China), NGAL (Bioporto, KIT 036, Denmark), and ADPN (R&D Systems, DRP300, USA). All assays were performed strictly according to the manufacturers' instructions.

Pathogen Identification and Antimicrobial Resistance Analysis

Clean midstream urine samples were collected at the time of suspected postoperative UTI onset. After centrifugation, the sediment was inoculated onto MacConkey agar plates and incubated at 35°C for 24 hours. Isolated strains were subsequently identified using a MALDI-TOF mass spectrometry system (microflex LT/SH, Bruker, Germany), with the Bruker Biotyper database. A match score of ≥ 2.0 was considered species-level identification, 1.7–2.0 was considered genus-level, and < 1.7 was considered unidentifiable. The bacterial species were named according to the latest classification standards of Bergey's Manual of Systematics of Bacteria and LPSN. Species with ≤ 2 isolates were categorized as "Others" in the results.

Antimicrobial susceptibility testing was performed using a bacterial susceptibility analyzer (VITEK 2 Compact, bioMérieux, France) combined with the disk diffusion method, following the 2023 Clinical and Laboratory Standards Institute guidelines for antimicrobial susceptibility testing.[23] The tested antibiotics included commonly used antimicrobial agents such as ampicillin (AMP, 10 μg), gentamicin (GEN, 10 μg), cefepime (30 μg), and LVX (5 μg), imipenem (IPM, 10 μg), ciprofloxacin (CIP, 5 μg), cefazolin (CZO, 30 μg), amikacin (30 μg), and amikacin (AMX, 25 μg). All identifications and antimicrobial susceptibility tests were quality controlled using ATCC reference strains [*E. coli* ATCC 25922, *Pseudomonas aeruginosa (P. aeruginosa)* ATCC 27853] to ensure the accuracy of the tests.

Urine cultures were semi-quantitative according to Kass's criterion: $\geq 10^5$ CFU/mL was considered positive; 10^4–10^5 CFU/mL was interpreted as infection when supported by clinical symptoms and abnormal urinalysis.

Resistance phenotypes were classified per the criteria of Magiorakos et al,[24] including: multidrug-resistant (MDR) strains-non-susceptible to ≥ 3 classes of antibiotics; extensively drug-resistant (XDR) strains—susceptible to ≤ 2 antibiotic classes; and pandrug-resistant (PDR) strains, resistant to all conventional antimicrobial agents.

Urinalysis

Urine collected on postoperative day 2 was analyzed for pH, specific gravity, protein, red blood cells, and WBC using a fully automated urine analyzer (UX-2000, Sysmex, Japan). Urine cytology and uroflowmetry were not included in this study.

Statistical Analysis

Statistical analyses were conducted using SPSS 26.0 software (IBM Corp., Armonk, NY, USA) and GraphPad Prism 8 (GraphPad Software, San Diego, CA, USA). The Shapiro–Wilk test was used to assess the normality of data distribution. Continuous variables following a normal distribution were expressed as $\bar{x} \pm s$ and compared between groups using an independent sample *t*-test. Categorical variables were presented as counts and percentages [n (%)] and analyzed using the chi-square test. Correlations between continuous variables were assessed using Pearson's correlation analysis for normally distributed data. The diagnostic performance of hs-CRP, HBP, NGAL, and ADPN for postoperative UTI was evaluated using receiver operating characteristic (ROC) curve analysis. Variables with $P<0.05$ in univariate analysis were included in a multivariate logistic regression model to identify independent risk factors for postoperative adverse outcomes. A two-tailed P-value < 0.05 was considered statistically significant.

Results

Comparison of General Characteristics

There were no statistically significant differences between the postoperative UTI group and the Non-UTI group regarding age, sex, body mass index (BMI), history of diabetes, history of hypertension, recurrence of stones, stone location, type of the stone, stone diameter, operation time, urine routine indicators, NLR, and serum uric acid levels ($P>0.05$). However, the WBC and NEU levels in the UTI group were significantly higher than those in the Non-UTI group, with statistically significant differences ($P<0.05$). In the UTI group, the average time interval between the occurrence of UTI and the surgery date was (3.80 ± 0.75) days. The most common postoperative clinical symptoms were frequent urination

(70.73%), pyuria (70.73%), urgency (65.85%), and dysuria (60.98%), with a fever incidence of 19.51%. The results are shown in Table 1.

Microbiological Characteristics of Postoperative UTI in Kidney Stone Patients

A total of 67 pathogenic bacteria were detected from the urine culture specimens of renal stone patients with UTI, including 40 Gram-negative bacteria (59.70%, predominantly *E. coli, P. aeruginosa*, and *K. pneumoniae*), 22 Gram-positive bacteria [32.84%, predominantly *Enterococcus* and *Staphylococcus aureus (S. aureus)*], and 5 fungi. All isolated *S. aureus* strains were methicillin-sensitive, and no vancomycin-resistant *enterococci* were detected, indicating that highly resistant Gram-positive strains are not currently widespread. All isolates were identified to the species level using the MALDI-TOF mass spectrometry system. The specific distribution of bacterial species is shown in Table 2.

Table 1 General Characteristics [$\bar{x} \pm s$, n (%)]

Variable		**Infection Group (n=41)**	**Non-Infection Group (n=89)**	***t/x*²**	***p***
Age (years)		52.76±8.49	53.03±7.12	0.19	0.85
Gender	Male	24 (58.54%)	43 (48.31%)	1.17	0.28
	Female	17 (41.46%)	46 (51.69%)		
BMI (kg/m²)		24.80±0.62	24.59±0.83	1.42	0.16
Diabetes	Yes	17 (41.46%)	46 (51.69%)	1.17	0.28
	No	24 (58.54%)	43 (48.31%)		
Hypertension	Yes	8 (19.51%)	14 (15.73%)	0.29	0.59
	No	33 (80.49%)	75 (84.27%)		
Recurrent Stone	Yes	6 (14.63%)	11 (12.36%)	0.13	0.72
	No	35 (85.37%)	78 (87.64%)		
Stone Location	Kidney	13 (31.71%)	34 (38.2%)	0.60	0.74
	Ureter Bladder	19 (46.34%) 9 (21.95%)	39 (43.82%) 16 (17.98%)		
Stone Type	Calcium oxalate	27 (65.85%)	57 (64.04%)	0.61	0.74
	Calcium phosphate Uric acid	8 (19.51%) 6 (14.63%)	22 (24.72%) 10 (11.24%)		
Stone Diameter (cm)	<2	13 (31.71%)	25 (68.29%)	0.18	0.67
	≥2	28 (68.29%)	64 (71.91%)		
Surgery Time (min)	<60	17 (41.46%)	40 (44.94%)	0.14	0.71
	≥60	24 (58.54%)	49 (55.06%)		
Urine pH		6.1 (5.9, 6.3)	6.1 (6.1, 6.2)	0.87	0.39
Urine specific gravity		1.017 (1.012, 1.023)	1.016 (1.012, 1.022)	0.46	0.64
Urine protein		0.08 (0.07, 0.09)	0.08 (0.07, 0.09)	0.13	0.90
Urine red blood cells		8 (8, 9)	8 (8, 9)	0.57	0.57
Urine white blood cells		7 (7, 8)	8 (7, 8)	1.08	0.28

(*Continued*)

Table 1 (Continued).

Variable		**Infection Group (n=41)**	**Non-Infection Group (n=89)**	***t/x*²**	***p***
WBC (×10⁹/L)		6.56±0.91	6.06±0.96	2.80	0.01
NEU (×10⁹/L)		3.75±0.69	3.43±0.69	2.47	0.02
NLR		2.37±0.59	2.18±0.60	1.68	0.10
Serum Uric Acid (μmol/L)		288.88±49.61	275.80±51.83	1.35	0.18
Time from surgery to UTI onset (day)		3.80±0.75	–		
Infection Symptoms	Urinary frequency	29 (70.73%)	–		
	Urgency	27 (65.85%)	–		
	Dysuria	25 (60.98%)	–		
	Pyuria	29 (70.73%)	–		
	Fever	8 (19.51%)	–		

Table 2 Microbiological Characteristics of UTI Patients (n=41)

Pathogen	**Number of Strains (n)**	**Proportion of Total Strains (%)**
Gram-negative Bacteria	40	59.70 (40/67)
E. coli	19	28.36 (19/67)
P. aeruginosa	9	13.43 (9/67)
K. pneumoniae	7	10.45 (7/67)
Proteus mirabilis	2	2.99 (2/67)
Acinetobacter baumannii	1	1.49 (1/67)
Others	2	2.99 (2/67)
Gram-positive Bacteria	22	32.84 (22/67)
Enterococcus spp.	11	16.42 (11/67)
S. aureus	7	10.45 (7/67)
Streptococcus pneumoniae	2	2.99 (2/67)
Others	2	2.99 (2/67)
Fungi	5	7.46 (5/67)
Candida albicans	3	4.48 (3/67)
Others	2	2.99 (2/67)

Antibiotic Resistance Analysis of Major Gram-Negative and Gram-Positive Bacteria

E. coli, P. aeruginosa, and *K. pneumoniae* exhibited high resistance to AMP (all >85%), but were all sensitive to imipenem (resistance rate 0%). *E. coli* demonstrated high resistance to GEN (68.42%), LVX (68.42%), and CIP (63.16%), while *K. pneumoniae* showed high resistance to cefoperazone (57.14%) and CZO (57.14%). Regarding Gram-positive bacteria, *Enterococcus* exhibited high resistance to cefoperazone (63.63%) and AMX (63.64%), and *S. aureus* showed high resistance to cefoperazone (42.86%). Overall, Gram-negative bacteria displayed significant resistance to AMP, while resistance patterns in Gram-positive bacteria showed some variations. The details are shown in Table 3.

Analysis of MDR/XDR Strains

Based on the international criteria proposed by Magiorakos et al, antimicrobial resistance profiles were analyzed for 67 isolated pathogenic strains. The results showed 14 MDR strains (22.58%), with *E. coli* (n = 6) and *K. pneumoniae* (n = 3)

Table 3 Antibiotic Resistance Analysis of Major Gram-Negative and Gram-Positive Bacteria

Antimicrobial Agents	*E. coli* (n=19)	*P. aeruginosa* (n=9)	*K. pneumoniae* (n=7)	*Enterococcus spp.* (n=11)	*S. aureus* (n=7)
	Resistance Rate %	**Resistance Rate %**	**Resistance Rate %**	**Resistance Rate %**	**Resistance Rate %**
Ampicillin (AMP)	17 (89.47%)	8 (88.89%)	6 (85.71%)	3 (27.27%)	2 (28.57%)
Gentamicin (GEN)	13 (68.42%)	5 (55.56%)	3 (42.86%)	2 (18.18%)	2 (28.57%)
Cefepime (FEP)	9 (47.37%)	4 (44.44%)	4 (57.14%)	7 (63.63%)	3 (42.86%)
Levofloxacin (LVX)	13 (68.42%)	3 (33.33%)	3 (42.86%)	3 (27.27%)	2 (28.57%)
Imipenem (IPM)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (27.27%)	3 (42.86%)
Ciprofloxacin (CIP)	12 (63.16%)	2 (22.22%)	2 (28.57%)	–	–
Cefazolin (CZO)	10 (52.63%)	3 (33.33%)	4 (57.14%)	4 (36.36%)	2 (22.22%)
Amikacin (AMK)	3 (15.79%)	2 (22.22%)	2 (28.57%)	–	–
Amoxicillin (AMX)	3 (15.79%)	2 (22.22%)	2 (28.57%)	7 (63.64%)	1 (14.29%)

Note: "–" indicates that the antibiotic was not used to carry out drug susceptibility tests.

being the most common. Additionally, 1 XDR strains (1.61%) were identified, primarily *P. aeruginosa* (n = 1). No PDR strains were detected in this study. See Table 4 for details.

Expression of Hs-CRP, HBP, NGAL, and ADPN in Postoperative UTI Patients

Serum levels of hs-CRP, HBP, and NGAL in the UTI group were significantly higher than those in the non-UTI group (all P<0.001). In contrast, the ADPN levels in the UTI group were significantly lower than those in the non-UTI group. These findings suggest that elevated levels of hs-CRP, HBP, and NGAL may be closely related to postoperative UTI, while the decrease in ADPN levels may play a protective role in the infection process. The details are shown in Table 5 and Figure 1.

Correlation Analysis of Hs-CRP, HBP, NGAL, and ADPN with Postoperative Infection-Related Inflammatory Markers

hs-CRP, HBP, and NGAL were all significantly positively correlated with WBC and NEU (r=0.6889–0.7697, P<0.0001), with NGAL showing the strongest correlation with WBC (r=0.7697, P<0.0001). hs-CRP had the highest correlation with

Table 4 Distribution of MDR/XDR Strains

Bacterial Species	Total Number of Isolates	MDR (%)	XDR (%)	PDR (%)
E. coli	19	6 (31.58%)	0	0
K. pneumoniae	7	3 (42.86%)	0	0
P. aeruginosa	9	2 (22.22%)	1 (11.11%)	0
Enterococcus spp.	11	2 (18.18%)	0	0
S. aureus	7	0	0	0
Others	7	1 (11.11%)	0	0
Total	62	14 (22.58%)	1 (1.61%)	0

Table 5 Expression of Hs-CRP, HBP, NGAL, and ADPN in Postoperative UTI Patients ($\bar{x} \pm s$)

Index	UTI Group	Non-UTI Group	t-value	p-value
hs-CRP (mg/L)	8.32±2.54	7.27±1.22	3.20	0.002
HBP (ng/mL)	42.59±5.79	36.17±4.34	7.03	<0.001
NGAL (ng/mL)	67.64±6.96	76.18±8.66	5.54	<0.001
ADPN (μg/mL)	7.95±1.84	10.74±1.65	8.63	<0.001

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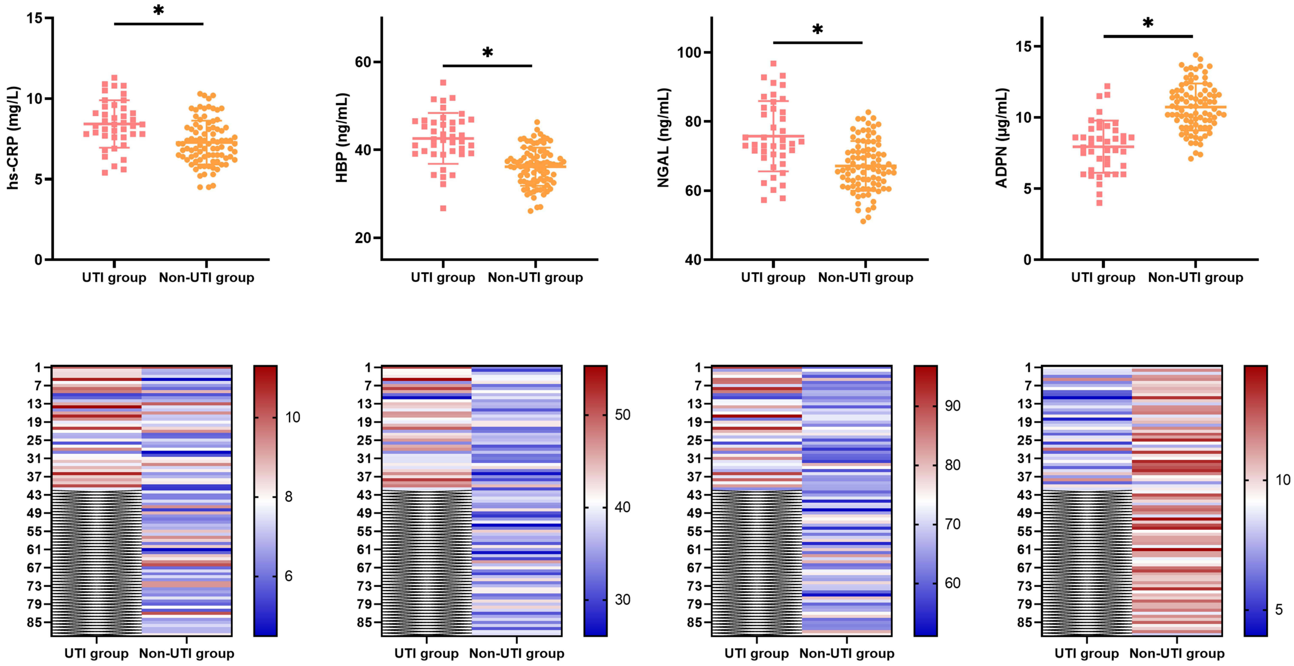

Figure 1 Expression levels of hs-CRP, HBP, NGAL, and ADPN in postoperative renal stone patients. *P < 0.001 vs Non-UTI group.

NEU (r=0.7298, P<0.0001). ADPN was significantly negatively correlated with both WBC and NEU (r = −0.7507 and −0.7212, P<0.0001), suggesting it may play a protective role during the infection process. See Table 6 and Figure 2.

Diagnostic Efficacy of Multiple Biomarkers for Postoperative UTI

To evaluate the diagnostic value of hs-CRP, HBP, NGAL, and ADPN in postoperative UTI in renal stone patients, ROC curve analysis was performed to assess the diagnostic efficacy of each biomarker. hs-CRP, HBP, NGAL, and ADPN all had certain diagnostic value when tested individually. The sensitivity and specificity were 75.28%/85.37% for HBP and 83.15%/78.05% for ADPN. NGAL (AUC = 0.7450) and hs-CRP (AUC = 0.7202) demonstrated moderate performance. When hs-CRP, HBP, NGAL, and ADPN were tested in combination, the diagnostic efficacy significantly improved (AUC=0.9496), with sensitivity and specificity reaching 92.13% and 90.24%, respectively, which were notably superior to those of individual markers. See Table 7 and Figure 3.

Risk Factors for Postoperative Adverse Outcomes

In the multivariate logistic regression analysis, postoperative UTI served as the dependent variable, with adjustments for potential confounders. HBP (P = 0.003, OR = 1.235, 95% CI: 1.073–1.421), NGAL (P = 0.005, OR = 1.137, 95% CI: 1.039–1.245), and ADPN (P<0.001, OR = 0.379, 95% CI: 0.234–0.613) were identified as independent predictors of

Table 6 Correlation Analysis of Hs-CRP, HBP, NGAL, ADPN with WBC and NEU in Postoperative Renal Stone Patients with UTI

Index	WBC		NEU	
	r	p	r	p
hs-CRP	0.6889	<0.0001	0.7298	<0.0001
HBP	0.7261	<0.0001	0.6885	<0.0001
NGAL	0.7697	<0.0001	0.7180	<0.0001
ADPN	−0.7507	<0.0001	−0.7212	<0.0001

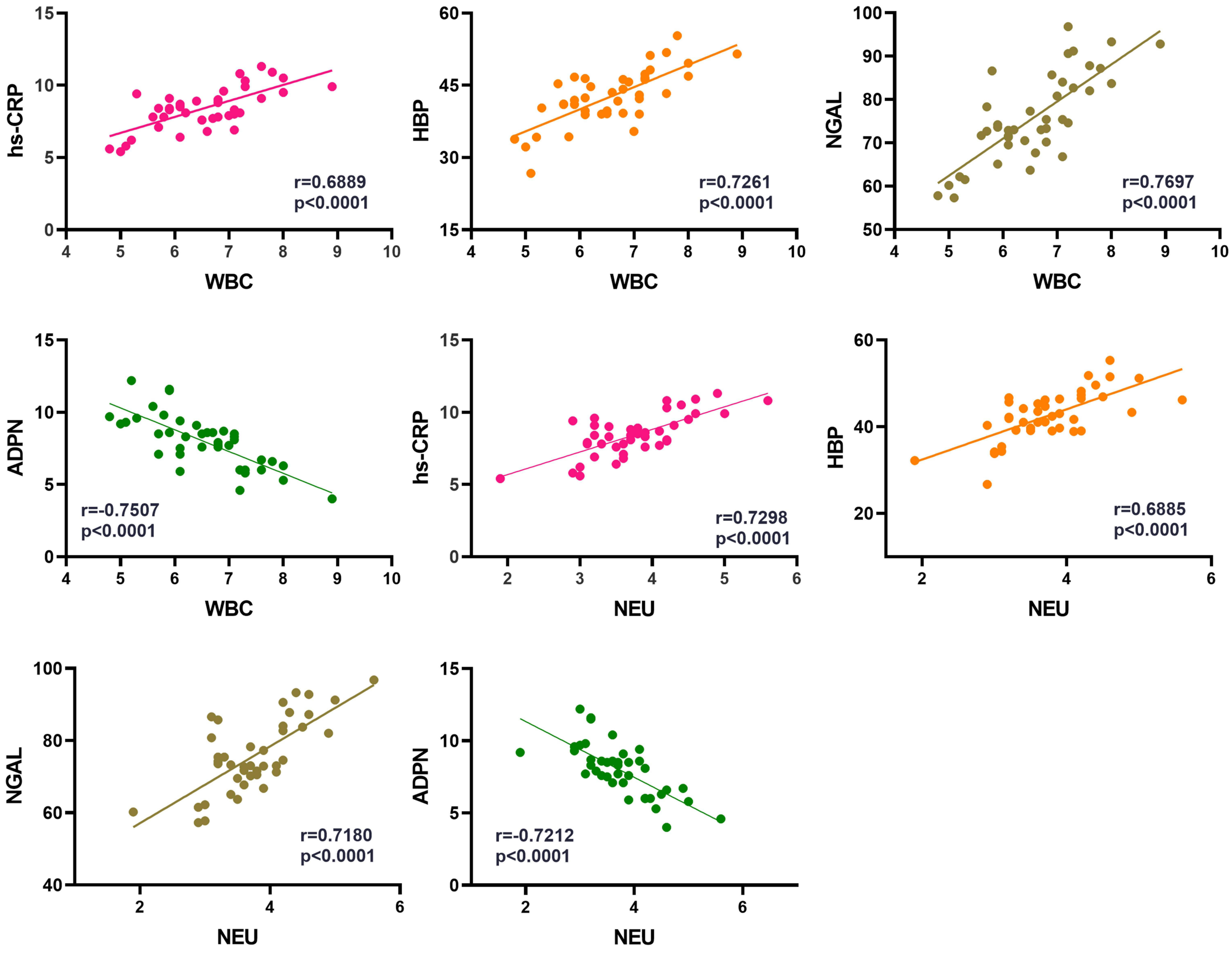

Figure 2 Pearson correlation analysis of hs-CRP, HBP, NGAL, ADPN with WBC and NEU.

postoperative infection. Elevated levels of HBP and NGAL significantly increased the risk of infection, while an increase in ADPN levels was associated with a decreased infection risk. These findings suggest that HBP, NGAL, and ADPN may play key roles in the pathogenesis of postoperative UTI (Table 8).

Discussion

This study systematically evaluated the distribution of pathogens and antibiotic resistance characteristics in UTI after renal stone surgery through urine culture and antibiotic sensitivity analysis. It also explored the diagnostic value of relevant inflammatory markers and risk factors for infection. In addition to the intrinsic antimicrobial resistance profiles of the pathogens, infection risk is also influenced by various clinical factors, including the presence of diabetes mellitus,

Table 7 Diagnostic Efficacy of Hs-CRP, HBP, NGAL, ADPN, and Their Combination for Postoperative UTI in Renal Stone Patients

Index	AUC	Sensitivity %	Specificity %	95% CI	Optimum Critical Value
hs-CRP	0.7202	65.17%	80.49%	0.6244–0.8160	<7.550
HBP	0.8193	75.28%	85.37%	0.7346–0.9040	<38.85
NGAL	0.7450	71.91%	70.73%	0.6496–0.8404	<71.20
ADPN	0.8719	83.15%	78.05%	0.8033–0.9404	>9.250
Combined diagnosis	0.9496	92.13%	90.24%	0.9095–0.9896	–

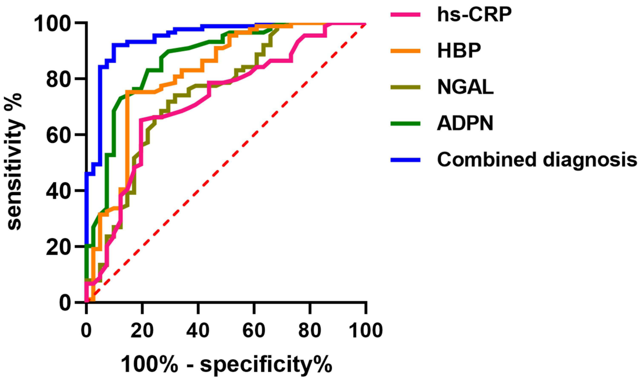

Figure 3 ROC curve evaluated the diagnostic efficacy of hs-CRP, HBP, NGAL, ADPN and combined tests.

immune status, existence of bilateral or complex stones, and postoperative catheterization. These factors may exacerbate the severity of infection by facilitating pathogen colonization and invasion.[25] Gram-negative bacteria predominated, with *E. coli, P. aeruginosa*, and *K. pneumoniae* as the leading pathogens.[26] Notably, Gram-negative bacteria exhibited a resistance rate to AMP exceeding 85%, while carbapenems still maintained over 90% sensitivity. This resistance pattern is consistent with the latest report from the national bacterial resistance monitoring network in China,[27] highlighting the clinical failure risk of AMP as an empirical treatment. In light of the 68.42% dual resistance of *E. coli* to GEN and LVX, combined with the 57.14% resistance of *K. pneumoniae* to third-generation cephalosporins, there is an urgent need to establish a stepwise treatment regimen, with β-lactamase inhibitor combinations at the core and carbapenems as backup. Among Gram-positive isolates, *Enterococcus* and *S. aureus* showed more than 40% resistance to cephalosporins, suggesting that glycopeptides or oxazolidinones should be considered as alternative treatment options. These results not only provide evidence-based guidance for perioperative antibiotic selection but also emphasize the necessity of establishing regional resistance monitoring networks and antibiotic stewardship programs. Moreover, the pathogenicity and infection propensity of different pathogens may be closely related to the expression of their virulence factors. For example, in *E. coli*, adhesins, iron acquisition systems, and cytotoxins play a critical role in attacking the urinary tract epithelium, which is pivotal in the occurrence and persistence of infection.[12]

Serological analyses revealed that hs-CRP, HBP, and NGAL levels were markedly elevated in the UTI group, while ADPN levels were decreased, reflecting a disturbed balance between pro- and anti-inflammatory responses.[28] HBP, as a specific product of NEU degranulation, directly represents the intensity of innate immune activation triggered by bacterial invasion.[29] Meanwhile, the dual elevation mechanism of NGAL may involve both tubular epithelial injury and NEU-mediated inflammatory cascades.[30] Conversely, ADPN exerts anti-inflammatory and metabolic regulatory functions; its reduction may aggravate infection by promoting macrophage M1 polarization[31] and insulin resistance, thereby facilitating bacterial proliferation.[32,33] Correlation analysis further revealed that the strong positive association between hs-CRP and NEU count underscores its role as a synchronous marker of systemic inflammatory response, whereas

Table 8 Analysis of Risk Factors for Postoperative UTI

Index	β	SE	Wald x^2	P	Exp (B)	95% CI
Constant	−17.425	5.554	9.844	0.002	0	–
WBC	0.392	0.335	1.37	0.242	1.48	0.767–2.855
NEU	1.009	0.616	2.683	0.101	2.742	0.82–9.17
hsCRP	0.301	0.261	1.326	0.25	1.351	0.81–2.253
HBP	0.211	0.072	8.673	0.003	1.235	1.073–1.421
NGAL	0.129	0.046	7.804	0.005	1.137	1.039–1.245
ADPN	−0.971	0.246	15.56	<0.001	0.379	0.234–0.613

NGAL's highest correlation with leukocyte count likely stems from its dual biological function in tissue repair and immune regulation.

ROC curve analysis demonstrated that HBP and ADPN exhibited the highest diagnostic performance, with AUC values of 0.8193 and 0.8719, respectively. The high sensitivity of HBP is attributed to its rapid release in the early stages of infection, whereas the high specificity of ADPN is closely related to its pivotal role in the metabolism-immune regulatory network.[34] When a diagnostic model incorporating hs-CRP, HBP, NGAL, and ADPN was constructed, the AUC increased to 0.9496, with sensitivity and specificity reaching 92.13% and 90.24%, respectively, significantly outperforming conventional single-marker assessments. This combinational approach enables a multidimensional analysis of the infection process: hs-CRP reflects systemic inflammatory burden, HBP indicates localized immune activation, NGAL signals renal parenchymal injury, and ADPN quantifies endogenous anti-inflammatory capacity. This integrative model not only enhances early detection of postoperative infections but also facilitates stratification of infection severity, providing a crucial biological basis for distinguishing uncomplicated UTIs from pre-septic states. It is noteworthy that the relationship between inflammatory markers and infection occurrence may vary among individuals, especially in patients with comorbidities or a history of urinary tract infections. Baseline inflammatory status may obscure early infection signals, suggesting that clinical assessment should incorporate individualized risk profiles by comprehensively considering factors such as pathogen type, prior medication history, and physiological condition.[35]

The multivariate logistic regression model confirmed that HBP and NGAL are independent risk factors for postoperative UTI, whereas ADPN served as a protective factor. An increase of 1 ng/mL in HBP corresponded to a 23.5% elevation in infection risk, potentially due to HBP-mediated alterations in vascular endothelial permeability and its role in facilitating bacterial dissemination.[34] The predictive value of NGAL reflects its dual function in the early warning of renal tubular injury and the surveillance of excessive NEU activation. The protective effect of ADPN suggests that strategies aimed at increasing preoperative ADPN levels, such as exercise interventions or PPAR-γ agonist therapy, may serve as novel approaches for infection risk reduction.[36] Notably, traditional inflammatory markers, such as white blood cell count, lost statistical significance in multivariate analysis, likely due to nonspecific elevations caused by surgical trauma. This finding further highlights the unique advantages of novel biomarkers in distinguishing postoperative infections. However, it should be noted that clinical baseline conditions such as renal function impairment, intraoperative blood loss, and timing of early catheter removal may also influence the release levels of HBP and NGAL, indicating that their stability should be further evaluated in more complex clinical contexts in future studies.

This study provides valuable insight into local antimicrobial resistance and proposes an evidence-based, biomarker-driven diagnostic approach. However, the study has several limitations. The small sample size and single-center design may limit generalizability. The absence of longitudinal biomarker monitoring restricted assessment of infection dynamics, and the predictive model did not include pathogen virulence or host genetic factors. Although species-level identification was achieved using MALDI-TOF, virulence profiling and molecular typing were not performed, leaving pathogen lineage-infection severity associations unclear. Future multicenter studies integrating metagenomic and multi-omics analyses, dynamic biomarker tracking, and AI-based individualized risk models are warranted. Additionally, exploring preoperative adiponectin modulation and elucidating HBP- and NGAL-related signaling mechanisms may advance precision prevention and treatment strategies for postoperative infections.

Conclusion

Postoperative UTI in kidney stone patients are primarily caused by Gram-negative bacteria. Combined detection of hs-CRP, HBP, NGAL, and ADPN significantly improves diagnostic accuracy. HBP, NGAL, and ADPN serve as early predictive markers of infection, providing a reference for clinical practice. It is recommended to implement combined biomarker testing in postoperative management and to develop individualized anti-infective strategies based on local antimicrobial resistance patterns. Future research may further integrate pathogen virulence typing and host inflammatory response mechanisms to explore more precise intervention approaches.

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Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

This study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Suzhou Hospital of Integrated Traditional Chinese and Western Medicine (No. 2025-008). Written informed consent was obtained from all participants.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

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