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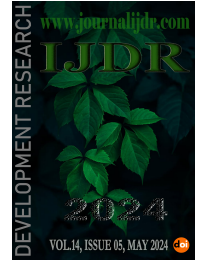
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RESEARCH ARTICLE

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EVALUATION OF ANTIBIOTIC EFFECTS IN HOSPITALIZED PATIENTS WITH URINARY TRACT INFECTION: A CROSS-SECTIONAL INVESTIGATION

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ABSTRACT

Objective: To identify predominant UTI-causing microorganisms in hospitalized patients, assess antibiotic effects on prognosis and hospital stay, and find favorable antibiotic alternatives for UTI management. **Methods:** We conducted a cross-sectional study of 189 adult UTI patients. Data on demographics, laboratory results, antibiotics, and hospital stays were collected. Stringent inclusion criteria were used. Multiple regression and statistical tests assessed hospitalization factors. **Results:** In the 18-95 age range, women showed a greater prevalence of UTIs (52.4%) than males (47.6%). The most common urine isolated microorganism was *Escherichia coli* (33.3%). High neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) (5.324 ± 3.055 and 174.979 ± 70.687) were detected. Carbapenems (5.92 days, 95% CI [0.271; 1.403]) were related with longer hospital stays than cephalosporins (3.98 days, 95% CI [-1.88; -1.124]). The study's model described 48% of hospital stay duration variance ($R^2=0.48$, $RMSE=0.19$, $p<0.001$). **Conclusion:** UTIs were found to be more common in women. The most common isolate (33.3%) was *E. coli*. Higher NLR and PLR levels show that inflammatory markers may be utilized as a clinical judgment of infection in patients. Cephalosporins were associated with shorter hospital stays (3.98 days) compared to quinolones (4.88 days) and carbapenems (5.92 days), indicating they may be a more effective antibiotic choice for UTIs to reduce hospitalization.

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INTRODUCTION

Urinary tract infections (UTIs) are among the most common bacterial infections, affecting millions annually. UTIs can lead to chronic kidney disease, hypertension, and other comorbidities, so early identification, effective treatment, and monitoring is critical for recovery (1, 2). Among the pathogens responsible for UTIs, *Escherichia coli* (*E. coli*), a gram-negative bacterium, ranks prominently as the most common nosocomial microorganism. The escalating use of antibiotics for treating UTIs in recent decades has raised concerns regarding the potential impingement on complete and sustainable long-term recovery. Some parameters, such as an inappropriate antibiotic treatment protocol for a causative agent, insufficient infection controls, and feed-added antibiotic use in animal production technology, have led to increased antibiotic resistance (2). To devise an optimal treatment regimen, it becomes imperative to thoroughly evaluate antibiotic resistance, taking into consideration factors such as the specific bacterial strain, clinical symptoms, infection localization, and progression. Thus, this study aimed to identify predominant UTI microorganisms in hospitalized patients as

well as to evaluate antibiotic impact on prognosis, the role of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio and length of stay and identify favorable antibiotics for effective management.

MATERIALS AND METHODS

Study Design

A retrospective cross-sectional study conducted at a city hospital in Isparta, Turkey between March 2018 and September 2019 evaluated antibiotic susceptibility in 189 adult UTI patients. The antibiotic treatment protocol used cephalosporins, quinolones, and carbapenems based on proven efficacy for UTI management. The Council for Appropriate and Rational Antibiotic Therapy CARAT (3) criteria were used to assess appropriateness of antibiotic usage. Compliance with the hospital's antibiotic policy was evaluated by considering indication, dosage, frequency, and duration of treatment.

Population and Sample Selection

Over 4-5k annual UTI cases were diagnosed and hospitalized at an 845-bed city hospital in Isparta, Turkey. G*Power software estimated a minimum of 68 patients needed for the study using parameters of 0.15 effect size, 80% power, 0.05 significance level, and 7 predictors. Initially, 270 eligible patients were selected, and reduced to 192 after applying exclusion criteria. After removing 3 outliers, the final 189 patients included 90 (47.6%) men and 99 (52.4%) women.

Data Collection

Patient data was sourced from the City Hospital's Information System for adult UTI admissions, including vital signs, demographics, urinalysis, microbiology, blood work, cultures, antibiotic sensitivity, CCI scores, presentations, admission/discharge dates, lengths of stay, and 30-day readmissions. Exclusion criteria filtered out UTI complications, pre-existing renal or urologic conditions, recent pregnancies, incarcerated individuals, immunocompromised patients, diabetes, steroids, biologics, or chemotherapy, recurrent UTIs, pre-prescribed antibiotics, and complicated cystitis or pyelonephritis. Data collection focused on assessing the appropriateness of UTI antibiotic prescriptions by comparing prescribed antibiotics, dosages, and durations to guidelines from IDSA, AAP, and UpToDate (3).

Ethical Consideration

We obtained written permission from the hospital to perform the research and conducted the study in accordance with the Helsinki Declaration. All participating patients were provided with comprehensive written information detailing the research's objectives and procedures, ensuring their clear understanding. Furthermore, prior to data collection, we secured written informed consent from each patient, affirming their voluntary participation and adherence to ethical research practices.

Statistical Analysis

Data normality and homogeneity of variances were assessed using Shapiro-Wilk and Bartlett's tests. Independent tests like Student's t-test, ANOVA, and non-parametric equivalents were used appropriately with Bonferroni corrections for ≥ 3 groups. Pearson correlation and multiple regression analyses were used for hospital stay length and antibiotic variables. Variables were assessed using dummy coding, stepwise selection, and best subset techniques. Model selection used the Akaike information criterion (AIC) the Bayesian information criterion (BIC), Mallow's Cp statistics, and adjusted R^2 . Validation used bootstrap and k-fold. 95% confidence intervals, $p < 0.05$ significance. All the statistical analyses were performed using R Statistical Software v. 4.1.2 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Descriptive values concerning the age, gender, and UTI distributions of patients are presented in Table 1. When the age distribution was examined, 27.5% were between 18 and 59 ($n = 52$), 26.5% were between 60 and 75 ($n = 50$), and 46% were between 76 and 96 ($n = 87$). Of the 189 patients, 52.4% were female ($n = 99$) and 47.6% were male ($n = 90$). According to the diagnosis, 97.3% ($n = 184$) of the patients were diagnosed with UTI only, and 2.7% ($n = 5$) reported at least one comorbidity.

Table 1. Age, gender, and distribution of the participants in the study

Individual Features		n (%)	%
Age (years)	18-59	52 (27.5)	27.5
	60-75	50 (26.5)	26.5
	76-96	87	46.0
Gender	Female	99	52.4
	Male	90	47.6

The dataset includes information on age range and gender distribution. Temperature data exhibited a non-normal distribution per Shapiro-Wilk's test. Temperatures were taken on arrival, days 3 and 6, and daily averages. Initially, 5 times per day for 72 hours, then reduced to 3 times until discharge. Analysis revealed a highly significant temperature difference across the 3 days ($p < 0.001$) as shown in 36, indicating the efficacy of treatment over time.

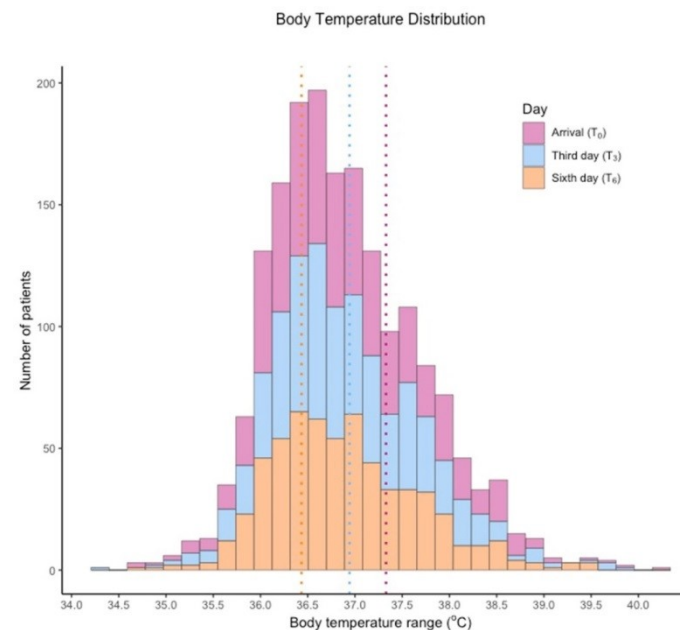


Figure 1. Histogram of body temperatures on arrival ($T_0 = 37.34^\circ\text{C}$), day 3 ($T_3 = 36.93^\circ\text{C}$), and day 6 ($T_6 = 36.43^\circ\text{C}$). A Wilcoxon signed-rank test with Bonferroni post-hoc analysis was used with 5% significance

CRP values decreased gradually over time ($p < 0.001$), and WBC values showed similar differences between days 1-3 and 1-6 ($p < 0.001$) but not between days 3-6 ($p = 0.98$). Higher NLR and PLR were observed at 5.324 ± 3.055 and 174.979 ± 70.687 , respectively. Results were significantly higher than non-UTI values of 2.541 ± 0.888 and 124.5477 ± 44.647 for NLR and PLR properties. Males had NLR values of 5.763 ± 6.415 , while females had 5.011 ± 5.497 . The PLR values for males were 139.566 ± 118.292 , whereas for females they were 129.572 ± 123.321 ($p < 0.001$). The study group's frequency and percentage distribution characteristics display urine culture details upon arrival, day 3, and day 6. Of 174 cases on arrival, 33.3% ($n = 58$) showed *E. coli*, the most dominant gram-negative bacteria (Table 2). *E. coli* growth occurred in 47 patients on day 3 and in 12 patients on day 6. Furthermore, the table also indicates decreasing microorganisms in blood cultures over time. On admission, of 75 cases, 10.7% ($n = 8$) had *E. coli*, a substantial gram-negative portion, and 16% ($n = 12$) had *Stap. spp.*, predominantly gram-positive bacteria.

Of 189 patients, 34.4% ($n = 65$) cephalosporin, 31.2% ($n = 59$) quinolone and 34.4% ($n = 65$) received carbapenem antibiotics intravenously. Patients given cephalosporins had shorter hospital stays compared to other groups. Figure 2 shows box plots representing the mean length of hospital stay for patients based on gender and antibiotics administered. The figure indicates cephalosporin antibiotics were associated with shorter stays for both genders. The average length of hospital stays for the selected antibiotic groups is presented in Table 3. The shortest hospital stays of patients who were administered cephalosporin serve as a reference.

Multiple Linear Regression

Multiple linear regression (MLR) models the relationship between multiple predictor variables and an observed outcome through linear equations.

$$y = \beta_0 + \beta_1x_1 + \beta_2x_2 + \beta_3x_3 + \dots + \beta_ix_i + \varepsilon \tag{1}$$

where y is the criterion variable LOS, β_0 is the intercept, β_{ii} the estimated regression coefficients for predictors x_i , and ε is the model error.

homogeneity test of variances indicated that the variances were equal among the antibiotics ($p = 0.228$). $*p < 0.05$. To identify the most suitable MLR model, we conducted a selection process, developing an optimal regression equation using these variables:

Table 2. The study group's frequency and percentage distribution characteristics

Urine culture results							
	Microorganism	On arrival <i>n</i> = 174		Day 3 <i>n</i> = 47		Day 6 <i>n</i> = 12	
		<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Gram-negative pathogen	<i>Escherichia coli</i>	58	33.3	-	-	-	-
	<i>Klebsiella</i> spp.	17	9.7	-	-	-	-
	<i>Enterobacter</i> spp.	4	2.4	1	2.1	1	8.3
	<i>Pseudomonas</i> spp.	3	1.7	-	-	-	-
	<i>Citrobacter freundii</i>	1	0.6	-	-	-	-
	<i>Acinetobacter B.</i>	-	-	-	-	1	8.3
	No growth	91	52.3	46	97.9	10	83.4
Gram-positive pathogen	<i>Staphylococcus</i> spp.	4	2.4	2	4.3	1	8.3
	<i>Enterococcus</i> spp.	5	2.9	3	6.4	1	8.3
	<i>Streptococcus</i> spp.	5	2.9	-	-	1	8.3
	<i>Bacillus</i> spp.	1	0.6	-	-	-	-
	No growth	159	91.2	42	89.4	9	75.1
Funguria	<i>Candida Albicans</i>	9	5.2	2	4.3	3	25.0
	<i>Candida Tropicalis</i>	1	0.6	-	-	1	8.3
	Yeast	-	-	-	-	1	8.3
	No growth	164	94.2	45	95.7	7	58.4
Blood culture results							
	Microorganism	<i>n</i> = 75		<i>n</i> = 8		<i>n</i> = 2	
		<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Gram- negative pathogen	<i>Escherichia coli</i>	7	14.30	1	12.5	-	-
	<i>Klebsiella</i> spp.	1	2.04	-	-	-	-
	No growth	41	83.7	7	87.5	2	100
Gram-positive pathogen	<i>Staphylococcus</i> spp.	12	18.50	2	25.0	-	-
	No growth	53	81.53	6	75.0	2	100
Funguria	<i>Candida Albicans</i>	-	-	-	-	-	-
	No growth	75	100	8	100	2	100

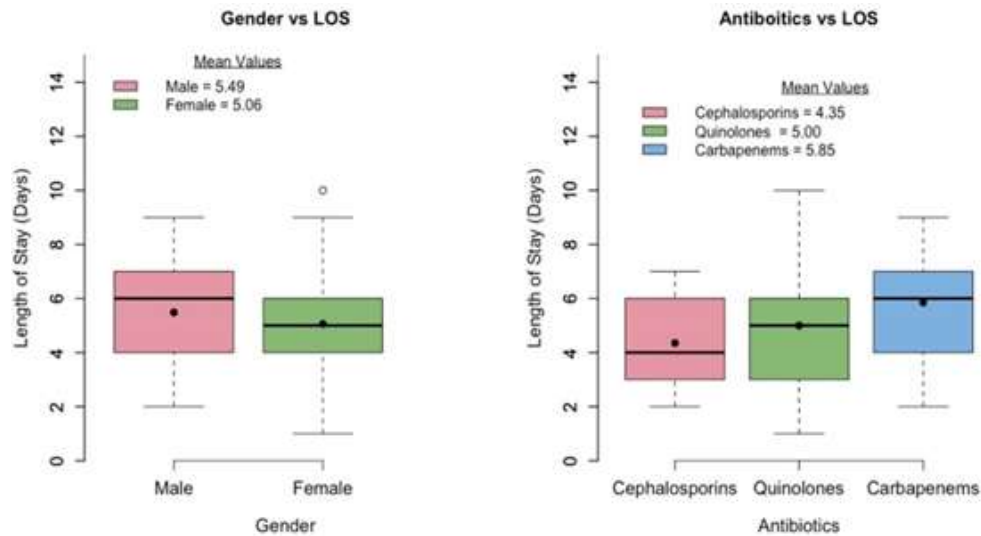


Figure 2. Boxplots of hospital stay by gender and antibiotic. Males had median stay of 6 days, females 5 days. By antibiotic: cephalosporins 4 days, quinolones 5 days, carbapenems 6 days. Means also displayed.

Table 3. Hospital stays data by antibiotic groups

Antibiotic Groups	<i>n</i>	Mean ± SD (LOS, Day)	Mean Rank	<i>p</i>
Carbapenems	65	5.85 ± 1.80	113.06	<0.001*
Quinolones	59	5.00 ± 2.50	96.58	0.065
Cephalosporins	65	4.35 ± 1.64	75.51	<0.001*
Total	189	5.03 ± 1.96	-	

Urine culture frequency and percentage at day 1, 3, and 6. *E. coli* is most common on arrival, decreasing UTI prevalence over time. The dataset was used to calculate the mean values with standard deviations and the mean rank of antibiotic groups. Fligner-Killeen's

- LOS (continuous),
- Age (continuous),
- Gender (Female = 0, Male = 1),
- WBCs (continuous),

- BTemps (continuous),
- CRPs (continuous),
- NRLs (continuous),
- PLRs (continuous),
- Antibiotic class (0 for Carbapenems, 1 for Quinolones, 2 for Cephalosporins).

Variance inflation factors were under 2, indicating low multicollinearity among the predictor variables in the regression model. Residual analysis revealed no distinct patterns in the scatterplot (Figure 3), meeting the assumption of homoscedasticity. With a sample size of 189, the study was sufficiently powered at 0.8 to detect medium-sized effects using multiple linear regression analysis with a significant level of 0.05.

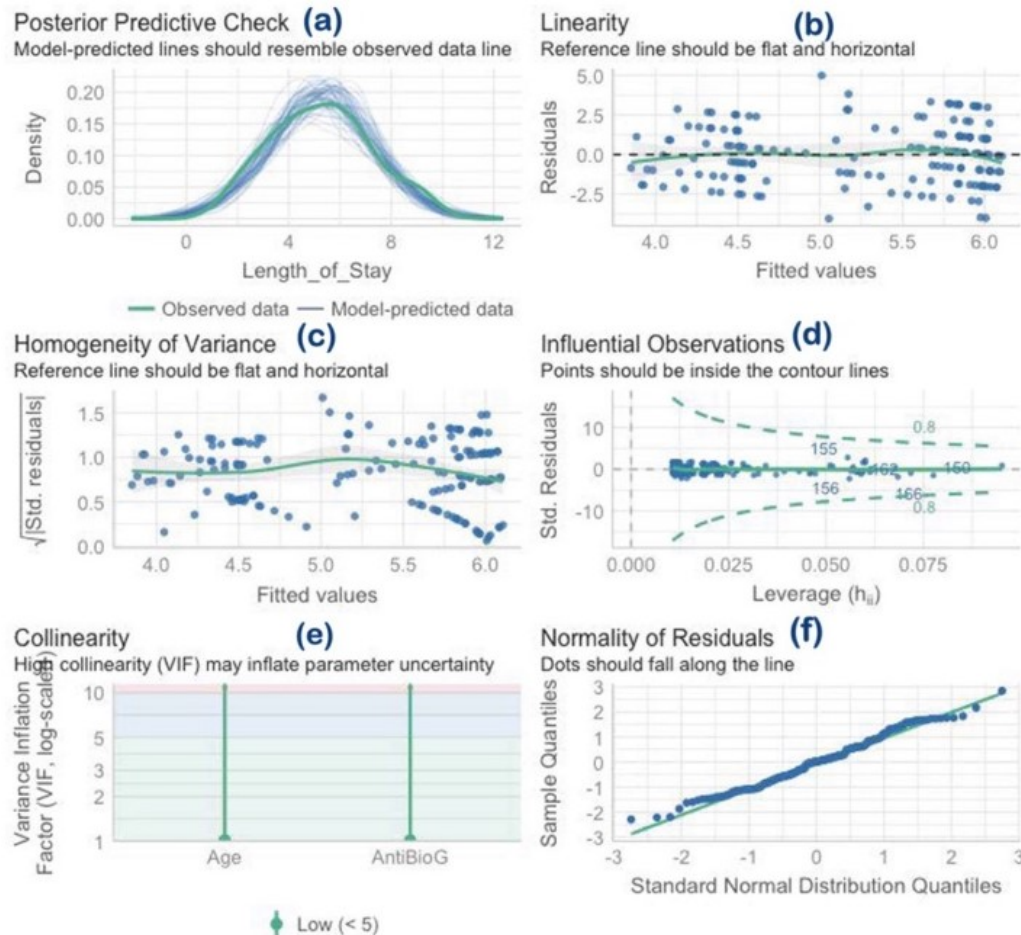


Figure 3. The steps to follow for the outcome variable length of stay vs. predictor variables age and antibiotics in an MLR. (a) Outcome variable length of stay is normally distributed. (b) Assesses linearity, equal variance, and independence. (c) Flat residual line indicates homogeneity. (d) Contour lines show data point influence on coefficients. (e) VIF close to 1 means no multicollinearity. (f) QQ plot checks normality of residuals

Model Evaluation Criteria

There are various parameters for choosing a model. These include R^2 , Root mean squared error (RMSE), Residual Standard Error (RSE), and mean absolute error (MAE). These criteria metrics raise issues since they penalize the result for model predictors that are added later. We used goodness of fit R^2 and $\text{Adj}R^2$, Akaike's Information Criteria, Bayesian Information Criteria, and Mallows' Cp as the evaluation measures for our model.

R^2 and Adjusted R^2

The coefficient of multiple determination, R^2 , which denotes the proportion of total variation in outcomes that can be attributed to the model, is a measure of how well the model reproduces observed outcomes.

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R^2 and Adjusted R^2

The coefficient of multiple determination, R^2 , which denotes the proportion of total variation in outcomes that can be attributed to the model, is a measure of how well the model reproduces observed outcomes.

$$R^2 = 1 - \frac{\text{Residual sum of squares}}{\text{Total sum of squares}} \text{ and } R^2 \text{Adj} = 1 - \frac{(n-1)}{(n-p)}(1 - R^2) \quad (2)$$

Where p is the total number of parameters. R^2 does not consider model complexity regarding the number of parameters fitted.

However, $\text{Adj}R^2$ does, but it penalizes adding independent variables that do not fit the model. With this criterion, the index value with the highest value is chosen.

Akaike's Information Criteria

$$\text{AIC} = -2 \log(\text{maximized likelihood}) + 2p = \frac{1}{n\hat{\sigma}^2} (\text{RSS} + 2d\hat{\sigma}) \quad (3)$$

where p is the number of parameters in the model, d is the number of predictors, $\hat{\sigma}^2$ is an estimate of the variance of an error (ϵ) and RSS is the sum of square error of the residual. Select the model that has the lowest AIC (and likely retain all models within 2 of the minimum). For small n , a corrected version of AIC (AIC_c) exists:

$$\text{AIC}_c = \text{AIC} + \frac{2p(p+1)}{n-p-1} \quad (4)$$

which has a higher penalty than AIC for smaller sample sizes and a higher penalty than BIC for very small sample sizes. The index with the smallest value is chosen.

Bayesian information criteria

$$BIC = -2 \log(\text{maximized likelihood}) + p \log(n) = \frac{1}{n} (RSS + \log(n) d\hat{\sigma}^2) \tag{5}$$

The only difference between BIC and AIC is the second term, which is dependent on sample size n. It is a variant of AIC. The model with the lowest index score is selected.

Mallows' Cp

$$C_p = \frac{1}{n} (RSS_p + 2d\hat{\sigma}) = \frac{RSS_p}{s^2 - (n - 2p)} \tag{6}$$

where RSSp is the residual sum of squares from a model containing p parameters, which includes s² and β₀. Mallows' Cp is almost a special case of AIC. One should look for models where Mallows' Cp is small and close to the number of predictors in the model plus the constant (p). A small Mallows' Cp value indicates that the model is relatively precise (has small variance) in estimating the true regression coefficients and predicting future responses. Models with lack-of-fit and bias have values of Mallows' Cp larger than p.

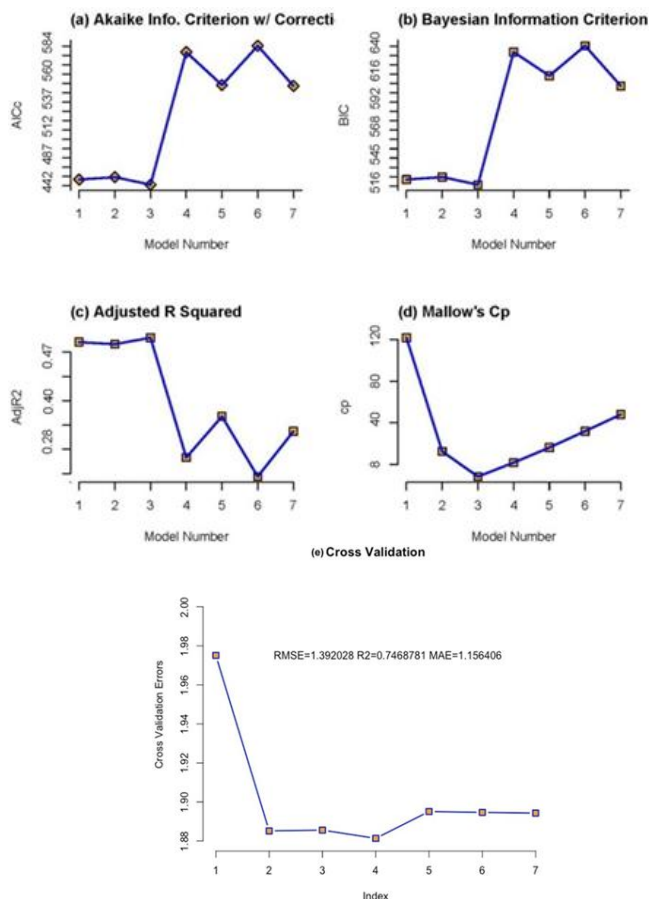


Figure 4. Model comparisons to determine the best fit. (a) Using the effectiveness of AICc, (b) BIC, (c) AdjR², and (d) MCp distinct models are displayed for comparison. (e) The error values were revealed through cross-validation of the selected models

We conducted a thorough examination using various techniques including indicator and contrast coding, selection methods like forward, backward, stepwise, and best subset to identify the most influential predictors for our regression model. To evaluate the performance of the model, we used the criteria mentioned earlier, which included R², Root Mean Square (RMSE), RSE, and Mean Absolute Error (MAE). Our priority was to maximize the adjusted R² while minimizing AICc, BIC, and RSS. We chose Model 3 as

optimal, with an adjusted R² of 48% shown in Figure 4. For an average age of 67.41 years, the estimated average length of stay (LOS) was 5.92 days for carbapenems, 4.88 days for quinolones, and 3.98 days for cephalosporins. The model achieved a moderate R² of 48.4%, indicating its ability to explain variations in hospital duration. The formula revealed that carbapenems were the most prescribed antibiotic (55.7%) with a length of stay (LOS) of 5.92 days, while cephalosporins had the shortest LOS at 3.98 days. Quinolones were found to be insignificant (p = 0.08) despite having a LOS of 4.88 days. The equation for the efficient LOS model is displayed in Table 4.

Table 4. Antibiotic groups regression data according to the length of hospital stay

Regression	Antibiotic Groups			Regression Equation
	r	AdjR ²	F	
Hospital Stays (Days)	0.695	0.473	37.32	5.17 + 0.011Age - 1.93 Cephalosporins

r: strength of the linear relationship, adjusted R²: proportion of the variation in the dependent variable.

In addition, the bootstrapping with 10k samples gave us slightly tighter confidence intervals versus original data. Cross-validation with 20% test 80% training produced similar results to the dataset (RMSE = 1.3921, R² = 0.484, MAE = 1.1564). Both validation methods aligned with our findings is displayed in Figure 4.

DISCUSSION

Urinary tract infections are influenced by various factors, including gender, age, symptomatic presentation, and underlying urinary system anomalies. Research by Geerlings SE *et al.* confirms the ubiquity of UTIs across age groups and genders. Women of all ages are particularly susceptible to UTIs, primarily due to their shorter urethra and the proximity of colon flora bacteria to the urethra (4). In the healthcare domain, patients with urinary catheters face an elevated risk of developing bacteriuria (5). Patel *et al.* also expressed that these infections typically result from pathogenic microorganisms such as *Escherichia coli*, *Klebsiella* spp., and *Enterobacter* spp. (6). In our study, *E. coli* was the most common microorganism isolated from urine cultures (33.3%, n = 58). Other gram-negatives such as *Klebsiella* spp. (9.8%, n = 17), *Enterobacter* spp. (2.4%, n = 4), *Pseudomonas* spp. (1.7%, n = 3), and *Citrobacter freundii* (0.6%, n = 1) were found in smaller percentages, with 52.3% (n = 91) showing no growth. On day 3 and 6 of treatment, gram-negative growth including *E. coli* was largely absent, indicating treatment effectiveness (6, 7). In blood cultures, *E. coli* (10.5%, n = 8) and *Staphylococcus* spp. (16%, n = 16) were the predominant initial isolates. By day 3 and 6, detection of these organisms declined substantially, consistent with previous research on common UTI isolates (4, 6, 7).

In bacterial infections, leukocyte count, and C-reactive protein levels rise and return to normal with treatment. CRP's role in diagnosing UTIs has been explored (6, 7), but its significance may vary in patients with renal dysfunction. In our study, CRP and WBC counts were elevated. CRP levels on the day of hospitalization were 9.90 ± 7.93, on day three (n = 153) 7.67 ± 7.83, and on day six (n = 102) 4.62 ± 5.03. WBC counts on arrival were 11.40 ± 5.49, on day three (n = 148) 8.38 ± 4.29, and on day six (n = 105) 8.30 ± 3.49. A recent study found UTI patients had significantly higher NLR (4.624 ± 5.818) and PLR (176.645 ± 110.051) versus non-UTI patients (NLR 2.117 ± 1.266, PLR 121.945 ± 53.735) (8). This aligns with previous research on elevated NLR and PLR in bacterial infections (9, 9). The increases likely reflect inflammation from infection. We found comparable results, with males having a higher NLR (5.763 ± 6.415) than females (5.011 ± 5.497). The increased NLR and PLR among males may indicate a more robust inflammatory response (8-9). Overall, NLR and PLR may serve as biomarkers to identify UTI patients and gauge inflammation (9). More research is warranted on using these ratios to guide UTI treatment and predict outcomes.

Quinolones and cephalosporins have historically been favored for treating UTIs due to their effectiveness, but rising resistance, as shown in prior studies (10), has reduced their efficacy. Consequently, healthcare providers are turning to more potent alternatives, with our study showing carbapenems accounting for a substantial 55.7% of prescribed antibiotics. It has potential as a primary UTI treatment (10, 11). Our findings support this trend, highlighting the strong preference for carbapenems in treating urinary tract infections apart from increasing antibiotic resistance. Quinolones and cephalosporins have historically been favored for treating UTIs due to their effectiveness, but rising resistance, as shown in prior studies (10), has reduced their efficacy. Consequently, healthcare providers are turning to more potent alternatives, with our study showing carbapenems accounting for a substantial 55.7% of prescribed antibiotics. It has potential as a primary UTI treatment (10, 11).

Our findings support this trend, highlighting the strong preference for carbapenems in treating urinary tract infections apart from increasing antibiotic resistance. Hospital length of stay (LOS) is a key factor in hospital-acquired infections. Trunfio *et al.* studied with 357 appendectomy patients underscores the importance of LOS in improving effectiveness and reducing costs (12). Our study reveals antibiotic class significantly impacts LOS in UTI patients. The average LOS was 5.27 ± 1.96 days, aligning with prior studies. A recent study reported a median UTI LOS of 3.5 days, shorter than our finding (13). Certain antibiotics reduced LOS, indicating their potential to expedite UTI recovery. Specifically, cephalosporins and quinolones were linked to 1.93 and 1.03 fewer hospital days versus carbapenems. Using multiple linear regression, we derived the following LOS prediction equation based on age and cephalosporin use:

$$LOS = 5.17 + 0.011Age - 1.93Cephalosporins$$

The model predicted LOS values of 3.98 days with cephalosporins, 4.88 days with quinolones (non-significant, $p = 0.08$), and 5.92 days with carbapenems, controlling for age. The model exhibited moderate fit ($R^2 = 0.48$) and was validated using bootstrapping and k-fold cross-validation. This predictive model is a valuable tool for estimating expected LOS based on patient factors and antibiotic choice.

Limitations

Our data may not fully capture differences between first-time and recurrent UTI patients suggested in prior research, which could affect model certainty and generalization. Further studies incorporating more diverse data on UTI recurrence could help enhance the model.

CONCLUSION

In conclusion, antibiotic therapy for UTI patients was examined, with *E. coli* as the predominant uropathogen. Elevated NLR and PLR in UTI patients, reflecting inflammation, could potentially serve as diagnostic criteria. Based on our observations, tests conducted on days 3 and 6 provided guidance for discharge timing and indicated that cephalosporins (3.98 days), quinolones (4.88 days), and carbapenems (5.92 days) are the most prescribed antibiotics. Despite carbapenems being preferred, appropriate antibiotics can reduce costs by decreasing the length of stay. Further large-scale research should examine demographics, comorbidities, and other factors influencing efficacy over time and settings.

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Conflict of Interest: The authors declare that they have no conflict of interest in the publication of this manuscript.

Ethical Approval: The Clinical Research Ethics Board of the Medical School at Suleyman Demirel University granted ethical approval for this study. Approval decision number 56 was released on May 2, 2019. All study steps were performed in accordance with Declaration of Helsinki.

Compliance with Ethical Standards: All the patients provided written informed consent prior to enrollment, and written informed consent was received from them for the study.

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Data Availability: Data available on reasonable request due to privacy or other restrictions.

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