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Evaluation of Systemic Pharmacotherapy in Bacterial Skin Infections: Adherence to Clinical Guidelines and Factors Associated with Treatment Outcomes

Lirim Shefki Mustafa [1], Arieta Hasani Alidema [2], Mirlinda Havolli [3], Linda Connelly [4] and Fitim Bexhet Alidema [1,*]

[1] Department of Pharmacology, Faculty of Pharmacy, UBT College, 10000 Prishtina, Kosovo
[2] Department of Nursing, Faculty of Medical, UBT College, 10000 Prishtina, Kosovo
[3] Faculty of Health Sciences, University of Maribor, 2000 Maribor, Slovenia
[4] Keigwin School of Nursing, Jacksonville University, Jacksonville, FL 32211, USA; lconnel@ju.edu
* Correspondence: fitim.alidema@ubt-uni.net

Abstract

Background: Bacterial skin infections frequently require systemic antibiotic therapy, and adherence to clinical guidelines is important for optimizing treatment outcomes and antimicrobial stewardship. This study evaluated systemic pharmacotherapy for bacterial skin infections, guideline adherence, and factors associated with treatment outcomes. Materials and Methods: This retrospective observational study included 300 patients treated in a regional hospital in Kosovo between January 2025 and August 2026. Demographic, clinical, laboratory, microbiological, and pharmacotherapeutic data were obtained from medical records. Guideline adherence and clinical outcomes were evaluated, and Firth penalized multivariable logistic regression was used to identify factors independently associated with guideline non-adherence and unfavorable clinical outcomes. Results: Guideline-adherent pharmacotherapy was documented in 269 patients (89.7%), while 266 (88.7%) achieved a favorable clinical outcome. Guideline non-adherence was independently associated with younger age (AOR 0.89 per year; 95% CI 0.83–0.95; $p < 0.001$), female sex (AOR 2.44; 95% CI 1.05–5.98; $p = 0.038$), higher CRP (AOR 1.23 per 10 mg/L increase; 95% CI 1.11–1.38; $p < 0.001$), and antibiotic modification (AOR 3.29; 95% CI 1.37–7.89; $p = 0.008$). Unfavorable clinical outcomes were independently associated with male sex (AOR 4.37; 95% CI 1.84–11.40; $p < 0.001$), higher CRP (AOR 1.22 per 10 mg/L increase; 95% CI 1.09–1.37; $p < 0.001$), intravenous administration (AOR 3.06; 95% CI 1.29–7.63; $p = 0.011$), and guideline non-adherence (AOR 3.12; 95% CI 1.16–8.23; $p = 0.025$). Conclusions: Guideline adherence and favorable clinical outcomes were high. Nevertheless, non-adherence remained independently associated with unfavorable outcomes, while higher CRP was associated with both study outcomes. These findings support continued optimization of systemic antibiotic pharmacotherapy and antimicrobial stewardship in dermatological practice.

Keywords: pharmacotherapy; systemic antibiotics; bacterial skin infections; clinical guideline adherence; antimicrobial stewardship; clinical outcomes

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1. Introduction

Bacterial skin and soft tissue infections represent a heterogeneous group of conditions ranging from superficial localized infections to more extensive and potentially severe disease requiring systemic antimicrobial treatment. Their clinical importance is related not

only to their high frequency but also to the considerable burden they impose on healthcare systems. Global epidemiological analyses indicate that bacterial skin diseases contribute substantially to the worldwide burden of skin disease, with marked differences in disease burden according to sociodemographic development [1]. More recent estimates indicate that the global burden of bacterial skin diseases remains substantial, with predictive models suggesting a continued rise in incidence rates and incident cases through 2045, emphasizing the need for effective prevention and treatment strategies [2].

The clinical spectrum of bacterial skin infections includes cellulitis, erysipelas, impetigo, folliculitis, furunculosis, abscesses, infected wounds, and other infections involving the skin and underlying soft tissues. The causative microorganisms vary according to the clinical presentation, anatomical site, patient characteristics, and healthcare exposure. *Staphylococcus aureus* remains one of the most important pathogens and is particularly prominent in purulent skin and soft tissue infections [3]. The emergence and dissemination of antimicrobial-resistant strains further complicate therapeutic decision-making, particularly in infections caused by Staphylococcus aureus, highlighting the clinical relevance of antimicrobial resistance patterns in the management of skin and soft-tissue infections [4].

Systemic pharmacotherapy plays a central role in the management of moderate and severe bacterial skin and soft-tissue infections and in cases in which local treatment alone is insufficient. Appropriate antimicrobial selection should be guided by the clinical characteristics of the infection and available evidence, while treatment duration represents an additional important component of therapeutic decision-making. Current recommendations increasingly emphasize appropriate antimicrobial selection, shorter effective treatment courses, and the integration of antimicrobial stewardship principles into the management of skin and soft-tissue infections [5]. These considerations are particularly relevant in dermatological practice, where antibiotics may be prescribed for a broad range of infectious and inflammatory conditions.

Despite the availability of evidence-based recommendations, inappropriate antibiotic prescribing remains an important concern. Deviations from recommended pharmacotherapy may include unnecessary use of broad-spectrum antibiotics, inappropriate antimicrobial selection, or treatment strategies that are not adequately supported by the clinical presentation. Evidence from patients with non-purulent skin and soft tissue infections has demonstrated that implementation of a guideline-based treatment algorithm can improve clinician adherence, reduce unnecessary antibiotic exposure, and reduce treatment failure and hospital readmission [6]. Pharmacist-driven implementation of antibiotic prescribing algorithms has demonstrated substantial improvements in guideline adherence, including more appropriate antibiotic selection, dosing, and treatment duration, highlighting the potential value of structured antimicrobial stewardship interventions [7].

Antimicrobial stewardship is particularly relevant in dermatology because antibiotic exposure may exert prolonged selective pressure on the cutaneous microbiome and contribute to the persistence of antimicrobial resistance [8]. Rational pharmacotherapy therefore requires balancing effective treatment with avoidance of unnecessary antimicrobial exposure. Stewardship strategies in dermatological practice include limiting unnecessary antibiotic use, selecting narrower-spectrum agents when appropriate, and prescribing the shortest effective treatment duration [5,8]. Strengthening antimicrobial stewardship in dermatology may consequently contribute to optimizing antibiotic use and reducing the risk of prolonged antimicrobial resistance in the skin [8].

2. Materials and Methods

2.1. Study Design, Setting, and Period

A retrospective, observational, and analytical study was conducted in the Department of Dermatology at the Regional Hospital in Gjilan, Kosovo, including patients treated between January 2025 and August 2026. Data were extracted from patients' medical, laboratory, and microbiological records and entered into a structured database for statistical analysis.

The study included 300 patients diagnosed with bacterial skin infections who received systemic antibiotic therapy during the study period. Each patient contributed a single observation corresponding to one treatment episode included in the analysis. Direct personal identifiers were excluded from the analytical database to ensure patient confidentiality.

2.2. Inclusion and Exclusion Criteria

Patients were eligible for inclusion if they had a documented diagnosis of a bacterial skin infection, received systemic antibiotic therapy as part of a documented therapeutic regimen for the treatment episode, and had sufficient medical documentation to evaluate their clinical characteristics, systemic pharmacotherapy, and treatment outcome. Both first episodes and recurrent bacterial skin infections were included.

Patients were excluded if the available medical records were insufficient to confirm the diagnosis, characterize the systemic antibiotic regimen, assess adherence to clinical guidelines, or determine the clinical outcome. Cases with incomplete or unreliable pharmacotherapeutic data that precluded a valid assessment of systemic antibiotic treatment were also excluded. Only records with complete documentation for the variables required for the study were included; consequently, there were no missing values among the 300 included patients, and no imputation of missing data was performed.

2.3. Data Collection and Study Variables

Data were extracted from patients' clinical, laboratory, and microbiological records using a structured data collection approach. Demographic and clinical variables included age, sex, primary dermatological diagnosis, anatomical site and type of infection, first or recurrent infection, body temperature at admission, and the presence of comorbidities.

Laboratory parameters included white blood cell count and C-reactive protein (CRP) concentration. Microbiological variables included whether a microbiological culture was performed, the culture result, and the microorganism identified in patients with a positive culture.

The collected variables were evaluated in relation to patterns of systemic antibiotic pharmacotherapy, adherence to clinical guidelines, and clinical treatment outcomes. This approach enabled an integrated assessment of demographic, clinical, laboratory, microbiological, and pharmacotherapeutic factors potentially associated with the two primary study outcomes.

2.4. Assessment of Systemic Pharmacotherapy

Systemic antibiotic pharmacotherapy was evaluated individually for each patient. Pharmacotherapeutic variables included the systemic antibiotic prescribed, dose, route of administration, treatment duration, use of monotherapy or combination therapy, and modification of the antibiotic regimen during treatment.

Patterns of systemic antibiotic use were assessed according to the primary dermatological diagnosis, clinical characteristics of the infection, laboratory parameters, and microbiological findings. Treatment was classified as monotherapy when a single systemic antibiotic was administered and as combination therapy when two systemic antibiotics

were used as part of the treatment regimen. Antibiotic treatment was considered modified when the initially prescribed antibiotic was replaced or the systemic antibiotic regimen was changed during the treatment episode. These pharmacotherapeutic characteristics were subsequently evaluated in relation to adherence to clinical guidelines and clinical treatment outcomes.

2.5. Assessment of Adherence to Clinical Guidelines

Adherence of systemic antibiotic pharmacotherapy was assessed individually for each treatment episode using a predefined, diagnosis-specific, evidence-based reference framework. The framework incorporated contemporary recommendations for the management of bacterial skin and soft-tissue infections, together with diagnosis-specific antimicrobial guidance where available. The assessment took into account the primary dermatological diagnosis, clinical presentation and severity of infection, microbiological findings when available, and the documented systemic antibiotic regimen.

For each patient, five pharmacotherapeutic components were evaluated: appropriateness of antibiotic selection, prescribed dose, route of administration, treatment duration, and use of monotherapy or combination therapy. Antibiotic selection was considered appropriate when the prescribed agent provided clinically appropriate antimicrobial coverage for the documented diagnosis and, where microbiological results were available, was compatible with the identified pathogen. Route of administration was evaluated in relation to the clinical severity of infection and the need for parenteral treatment, while treatment duration and dosing were assessed against the recommended ranges for the corresponding clinical condition.

The reference framework was primarily based on contemporary evidence-based recommendations for skin and soft-tissue infections, including the 2018 World Society of Emergency Surgery/Surgical Infection Society Europe (WSES/SIS-E) consensus recommendations [9] and diagnosis-specific antimicrobial prescribing guidance from the National Institute for Health and Care Excellence (NICE) for cellulitis and erysipelas, where applicable [10]. No formal local or institutional antimicrobial treatment protocol for the included bacterial skin infections was available during the study period; therefore, guideline adherence was evaluated against this international evidence-based reference framework rather than against a local institutional protocol. For dermatological bacterial conditions not specifically addressed by these guidelines, assessment was based on contemporary peer-reviewed dermatological and infectious-disease literature describing accepted systemic treatment approaches.

A treatment episode was classified as guideline-adherent when all evaluated components of systemic pharmacotherapy were consistent with the applicable recommendations. Non-adherence was defined as the presence of at least one clinically relevant deviation in antibiotic selection, dose, route of administration, treatment duration, or use of combination therapy. Guideline adherence was treated as one of the two primary study outcomes. The resulting binary classification of guideline-adherent versus non-adherent pharmacotherapy was examined in relation to demographic, clinical, laboratory, microbiological, and pharmacotherapeutic characteristics, and guideline non-adherence was used as the dependent outcome in the corresponding univariable and multivariable logistic regression analyses.

2.6. Assessment of Clinical Outcomes

Clinical outcome was determined from the medical documentation available at the end of treatment and was classified according to the documented clinical response. Outcomes were categorized as complete recovery, clinical improvement, or no clinical change.

For the analytical assessment of treatment outcomes, complete recovery and clinical improvement were combined and classified as a favorable clinical outcome, whereas no clinical change was classified as an unfavorable clinical outcome. This binary classification was used as the dependent outcome in the corresponding logistic regression analyses.

Clinical outcomes were evaluated in relation to demographic and clinical characteristics, inflammatory and microbiological parameters, and systemic pharmacotherapy. Treatment duration, route of administration, use of monotherapy or combination therapy, antibiotic modification during treatment, and adherence to clinical guidelines were examined as potential factors associated with treatment outcome.

2.7. Statistical Analysis

Data were analyzed using descriptive and inferential statistical methods. Categorical variables were summarized as frequencies and percentages, whereas continuous variables were presented as mean and standard deviation or median and interquartile range (IQR), according to their distribution. Associations between categorical variables were assessed using Pearson's chi-square test or Fisher's exact test, as appropriate. Continuous variables were compared between groups using parametric or non-parametric tests according to their distribution. The association between guideline adherence and the three-category clinical outcome (complete recovery, clinical improvement, and no clinical change) was additionally assessed using the Fisher–Freeman–Halton exact test because of the small expected cell frequencies in the 2×3 contingency table.

Logistic regression analysis was performed for the two primary binary outcomes: guideline non-adherence and unfavorable clinical outcome. Univariable analyses were initially conducted to examine associations between individual demographic, clinical, laboratory, microbiological, and pharmacotherapeutic variables and each study outcome. Variables showing statistically significant associations in univariable analyses, together with variables considered clinically relevant to each outcome, were considered for inclusion in the multivariable models. Given the relatively limited number of outcome events (31 cases of guideline non-adherence and 34 unfavorable clinical outcomes), parsimonious multivariable models were constructed to reduce the risk of overfitting and to identify factors independently associated with each outcome. Variables representing closely related clinical, inflammatory, or treatment-related constructs were not entered simultaneously when substantial correlation or redundancy was present. CRP was retained as the principal inflammatory marker because of its clinical interpretability and its consistent association with both study outcomes. To reduce small-sample bias associated with the limited number of outcome events, multivariable analyses were performed using Firth penalized logistic regression rather than conventional maximum-likelihood logistic regression. The same parsimonious covariate structure was retained to preserve clinical interpretability while limiting model complexity. The guideline non-adherence model included age, sex, CRP, and antibiotic modification during treatment, whereas the unfavorable clinical outcome model included sex, CRP, intravenous administration, and guideline non-adherence. For both study outcomes, associations identified in univariable analyses were expressed as odds ratios (ORs), whereas estimates from the Firth penalized multivariable logistic regression models were reported as adjusted odds ratios (AORs), with corresponding 95% confidence intervals (95% CIs). CRP was entered into the multivariable models as a continuous variable, and its effect estimates were expressed per 10 mg/L increase to facilitate clinical interpretation.

Body temperature ≥ 38 °C and performance of microbiological culture, which showed complete separation of the outcome categories, were not added to the primary multivariable models. The models were intentionally restricted to the selected parsimonious

covariate sets to avoid unnecessary model expansion given the limited number of outcome events. Model discrimination was assessed using the area under the receiver operating characteristic curve (AUC). Statistical analyses were performed using Python version 3.13.5 (Python Software Foundation), with pandas version 2.2.3 and NumPy version 2.3.5 for data management and numerical processing, SciPy version 1.17.0 for statistical testing, statsmodels version 0.14.6 for conventional logistic regression analyses, and scikit-learn version 1.8.0 for receiver operating characteristic analysis and calculation of the AUC. Firth penalized logistic regression was implemented using Jeffreys-prior penalized likelihood estimation. All statistical tests were two-sided, and a p-value < 0.05 was considered statistically significant.

2.8. Ethical Considerations

Ethical approval for this retrospective study was granted by the Department for Research and Ethical Affairs of the General Hospital in Gjilan (Protocol No. LH008/2026; approval date: 15 May 2026). The approval authorized the review and use of medical records from patients treated at the Department of Dermatology for the purposes of the present study. The study involved exclusively retrospective analysis of previously recorded medical data and included no additional diagnostic or therapeutic interventions.

Patient confidentiality and privacy were maintained throughout data collection, processing, and analysis. Direct personal identifiers were excluded from the analytical database, and all study data were handled in a manner designed to prevent individual patient identification and were used exclusively for research purposes.

The study was conducted in accordance with established ethical principles for medical research, the World Medical Association Declaration of Helsinki, as revised in 2013, and applicable institutional requirements regarding confidentiality and data protection.

3. Results

The final analysis included 300 patients with bacterial skin infections who received systemic antibiotic therapy. The mean age was 29.2 $\pm$ 6.7 years, and the sex distribution was nearly balanced. A first episode of infection was recorded in 198 patients (66.0%), whereas 102 (34.0%) had recurrent infection. Microbiological culture was performed in 207 patients (69.0%), with *Staphylococcus aureus* and *Streptococcus pyogenes* representing the most frequently isolated microorganisms. Amoxicillin/clavulanate, cephalexin, and clindamycin were among the most commonly prescribed systemic antibiotics. Oral administration predominated in 210 patients (70.0%), whereas 90 (30.0%) received intravenous treatment. Monotherapy was used in 83.3% of cases, and antibiotic modification during treatment was documented in 17.3%. Overall, 269 patients (89.7%; 95% CI 85.7–92.6) received pharmacotherapy classified as adherent to clinical guidelines, whereas 31 (10.3%) received non-adherent treatment. At the end of treatment, 131 patients (43.7%) achieved complete recovery, 135 (45.0%) showed clinical improvement, and 34 (11.3%) showed no clinical change. For outcome analyses, complete recovery and improvement were classified as favorable outcomes, whereas no clinical change was classified as an unfavorable outcome. Bivariable analyses identified several clinical and pharmacotherapeutic characteristics associated with guideline non-adherence and unfavorable clinical outcome. Multivariable models were subsequently used to determine which associations remained independent after adjustment for other covariates.

The study population consisted predominantly of young adults and showed a nearly balanced sex distribution. Comorbidity and associated clinical characteristics were recorded retrospectively as documented in the patients' clinical records. For the present analysis, these data were coded as mutually exclusive categories; therefore, the categories shown

in Table 1 sum to the total study population (n = 300) and should not be interpreted as investigator-defined primary comorbidities.

Table 1. Demographic and clinical characteristics of the study population (n = 300).

Characteristic	*n* (%) or Value
Age, years, mean ± SD	29.2 ± 6.7
Age, median (IQR), years	30 (23–35)
Male	154 (51.3)
Female	146 (48.7)
First episode of infection	198 (66.0)
Recurrent infection	102 (34.0)
No recorded comorbidities	88 (29.3)
Smoking	63 (21.0)
Obesity	63 (21.0)
Type 1 diabetes mellitus	30 (10.0)
Type 2 diabetes mellitus	27 (9.0)
Atopic dermatitis	29 (9.7)

The distribution of primary dermatological diagnoses is presented in Table 2.

Table 2. Distribution of primary dermatological diagnoses.

Diagnosis	*n* (%)
Cellulitis	28 (9.3)
Erysipelas	26 (8.7)
Carbuncle	16 (5.3)
Acute paronychia	16 (5.3)
Surgical wound infection	16 (5.3)
Periorbital cellulitis	16 (5.3)
Bacterial lymphangitis	16 (5.3)
Secondary infection of a traumatic wound	16 (5.3)
Infection of a chronic skin ulcer	16 (5.3)
Erysipeloid	16 (5.3)
Erythrasma	16 (5.3)
Trichomycosis axillaris	16 (5.3)
Pitted keratolysis	16 (5.3)
Impetigo	14 (4.7)
Folliculitis	14 (4.7)
Furunculosis	14 (4.7)
Cutaneous abscess	14 (4.7)
Ecthyma	14 (4.7)

Clinical, laboratory, and microbiological characteristics are summarized in Table 3.

Table 3. Clinical, laboratory, and microbiological profile.

Parameter	Result
Body temperature, °C, median (IQR)	37.75 (36.9–38.8)
Body temperature, range, °C	36.4–40.0
White blood cell count, $\times 10^9$/L, median (IQR)	9.9 (7.4–14.8)
CRP, mg/L, median (IQR)	9.2 (4.3–69.0)
Microbiological culture performed	207 (69.0)
Microbiological culture not performed	93 (31.0)

The diagnostic spectrum was heterogeneous and included superficial, deep, purulent, and wound-associated bacterial infections. Cellulitis and erysipelas were the two most frequent individual diagnoses and together accounted for 18.0% of the study population. The broad distribution of diagnoses allowed systemic pharmacotherapy to be evaluated across several clinically distinct bacterial dermatological conditions.

Inflammatory parameters showed considerable variability across the study population. CRP demonstrated a particularly wide distribution, ranging from 0.5 to 129.9 mg/L, consistent with substantial heterogeneity in inflammatory activity. Microbiological culture was performed in more than two-thirds of patients, providing an important basis for assessment of the etiological profile. The distribution of microorganisms isolated from microbiological cultures is presented in Table 4.

Table 4. Microorganisms isolated among patients who underwent microbiological culture (n = 207).

Microorganism	*n* (%)
Staphylococcus aureus	78 (37.7)
Streptococcus pyogenes	44 (21.3)
MRSA	17 (8.2)
Corynebacterium spp.	17 (8.2)
Pseudomonas aeruginosa	13 (6.3)
Erysipelothrix rhusiopathiae	11 (5.3)
Corynebacterium minutissimum	11 (5.3)
Escherichia coli	8 (3.9)
Kytococcus sedentarius	5 (2.4)
Klebsiella pneumoniae	3 (1.4)

Staphylococcus aureus was the predominant pathogen, accounting for 37.7% of isolates, followed by *Streptococcus pyogenes* at 21.3%. MRSA was identified in 17 cases, corresponding to 8.2% of patients who underwent microbiological culture. Gram-negative organisms were less frequent, although *Pseudomonas aeruginosa* accounted for 6.3% of isolates. The characteristics of systemic pharmacotherapy are summarized in Table 5.

Table 5. Characteristics of systemic pharmacotherapy.

Characteristic	*n* (%)
Amoxicillin/clavulanate	48 (16.0)
Cephalexin	40 (13.3)
Clindamycin	31 (10.3)
Cefazolin	21 (7.0)
Penicillin V	20 (6.7)
Erythromycin	20 (6.7)
Doxycycline	19 (6.3)
Penicillin G	18 (6.0)
Ceftriaxone	15 (5.0)
Clarithromycin	12 (4.0)
Other regimens	56 (18.7)
Oral administration	210 (70.0)
Intravenous administration	90 (30.0)
Monotherapy	250 (83.3)
Combination therapy	50 (16.7)
Antibiotic modification during treatment	52 (17.3)
No antibiotic modification	248 (82.7)
Treatment duration: 5 days	70 (23.3)
Treatment duration: 7 days	122 (40.7)
Treatment duration: 10 days	51 (17.0)
Treatment duration: 14 days	57 (19.0)

Systemic pharmacotherapy involved several antimicrobial classes, with amoxicillin/clavulanate representing the most frequently prescribed individual regimen. Oral administration predominated, whereas approximately one-third of patients received intravenous therapy. Monotherapy was the principal treatment strategy, and antibiotic modification during treatment occurred in 17.3% of patients. A seven-day course was the most common treatment duration. Guideline adherence and clinical outcomes are presented in Table 6.

Most systemic pharmacotherapy regimens were classified as adherent to clinical guidelines, and a favorable clinical outcome was documented in 88.7% of patients. Clinical outcome distribution differed significantly according to guideline adherence (Fisher–Freeman–Halton exact test, $p = 0.004$). Among patients receiving guideline-adherent pharmacotherapy, 43.5% achieved complete recovery, 47.2% showed clinical improvement, and 9.3% showed no clinical change. Among patients receiving non-adherent pharmacotherapy, the corresponding proportions were 45.2%, 25.8%, and 29.0%, respectively. The principal difference was observed in the proportion of patients with no clinical change, which was substantially higher among those receiving non-adherent pharmacotherapy. Factors associated with guideline non-adherence in the univariable analysis are presented in Table 7.

Table 6. Adherence to clinical guidelines and treatment outcomes.

Outcome	*n* (%)	95% CI
Guideline-adherent pharmacotherapy	269 (89.7)	85.7–92.6
Non-adherent pharmacotherapy	31 (10.3)	7.4–14.3
Complete recovery	131 (43.7)	—
Clinical improvement	135 (45.0)	—
No clinical change	34 (11.3)	8.2–15.4
Favorable clinical outcome	266 (88.7)	84.6–91.8
Unfavorable clinical outcome	34 (11.3)	8.2–15.4
Clinical outcome according to guideline adherence		
Complete recovery—adherent	117/269 (43.5)	—
Complete recovery—non-adherent	14/31 (45.2)	—
Clinical improvement—adherent	127/269 (47.2)	—
Clinical improvement—non-adherent	8/31 (25.8)	—
No clinical change—adherent	25/269 (9.3)	—
No clinical change—non-adherent	9/31 (29.0)	—

Table 7. Factors associated with non-adherence to systemic pharmacotherapy guidelines in univariable analysis.

Factor	Non-Adherent	Adherent	OR (95% CI)/Comparison	*p*-Value
Age, median (IQR), years	24.0 (21.0–31.5)	30.0 (24.0–35.0)	—	0.004
Female sex	21/146 (14.4%)	125/146 (85.6%)	2.42 (1.10–5.33)	0.025
Recurrent infection	14/102 (13.7%)	88/102 (86.3%)	1.69 (0.80–3.59)	0.166
White blood cell count, median (IQR)	15.3 (13.4–16.2)	9.5 (7.1–13.9)	—	<0.001
CRP, median (IQR), mg/L	70.6 (49.6–97.8)	8.0 (4.0–64.0)	—	<0.001
Intravenous administration	19/90 (21.1%)	71/90 (78.9%)	4.42 (2.04–9.55)	<0.001
Combination therapy	8/50 (16.0%)	42/50 (84.0%)	1.88 (0.79–4.48)	0.149
Antibiotic modification	15/52 (28.8%)	37/52 (71.2%)	5.88 (2.68–12.89)	<0.001
Treatment duration, median (IQR), days	10 (7–14)	7 (5–10)	—	<0.001

Guideline non-adherence was significantly associated with younger age, higher white blood cell counts, higher CRP concentrations, intravenous antibiotic administration, antibiotic modification, and longer treatment duration. Patients receiving intravenous therapy had 4.42-fold higher odds of guideline non-adherence (OR 4.42, 95% CI 2.04–9.55; $p < 0.001$), while antibiotic modification was associated with 5.88-fold higher odds (OR 5.88, 95% CI 2.68–12.89; $p < 0.001$). Female sex was also associated with higher odds of non-adherence in the univariable analysis (OR 2.42, 95% CI 1.10–5.33; $p = 0.025$). Recurrent infection and combination therapy were not significantly associated with guideline non-adherence. Factors associated with an unfavorable clinical outcome in the univariable analysis are presented in Table 8.

Table 8. Factors associated with an unfavorable clinical outcome in univariable analysis.

Factor	Unfavorable Outcome	Favorable Outcome	OR (95% CI)/Comparison	*p*-Value
Age, median (IQR), years	27.5 (21.3–35.8)	30.0 (23.0–35.0)	—	0.399
Male sex	24/154 (15.6%)	130/154 (84.4%)	2.51 (1.16–5.45)	0.017
Recurrent infection	11/102 (10.8%)	91/102 (89.2%)	0.92 (0.43–1.97)	0.830
White blood cell count, median (IQR)	15.0 (13.5–16.8)	9.5 (7.1–13.8)	—	<0.001
CRP, median (IQR), mg/L	77.0 (46.6–108.1)	7.9 (3.9–64.0)	—	<0.001
Intravenous administration	24/90 (26.7%)	66/90 (73.3%)	7.27 (3.31–16.00)	<0.001
Combination therapy	9/50 (18.0%)	41/50 (82.0%)	1.98 (0.86–4.54)	0.103
Antibiotic modification	7/52 (13.5%)	45/52 (86.5%)	1.27 (0.52–3.10)	0.594
Guideline non-adherence	9/31 (29.0%)	22/31 (71.0%)	3.99 (1.66–9.61)	0.001
Treatment duration, median (IQR), days	10 (10–14)	7 (5–10)	—	<0.001

An unfavorable clinical outcome was significantly associated with male sex, higher white blood cell counts, higher CRP concentrations, intravenous antibiotic administration, guideline non-adherence, and longer treatment duration. Intravenous administration was associated with 7.27-fold higher odds of an unfavorable clinical outcome (OR 7.27, 95% CI 3.31–16.00; $p < 0.001$), while guideline non-adherence was associated with approximately fourfold higher odds (OR 3.99, 95% CI 1.66–9.61; $p = 0.001$). Male sex was also associated with higher odds of an unfavorable outcome (OR 2.51, 95% CI 1.16–5.45; $p = 0.017$). Age, recurrent infection, combination therapy, and antibiotic modification were not significantly associated with clinical outcome in the univariable analysis. The Firth penalized multivariable logistic regression analysis of factors independently associated with guideline non-adherence is presented in Table 9.

Table 9. Firth penalized multivariable logistic regression analysis of factors associated with non-adherence to systemic pharmacotherapy guidelines.

Factor	AOR	95% CI	*p*-Value
Age, per additional year	0.89	0.83–0.95	<0.001
Female sex	2.44	1.05–5.98	0.038
CRP, per 10 mg/L increase	1.23	1.11–1.38	<0.001
Antibiotic modification	3.29	1.37–7.89	0.008

In the Firth penalized multivariable model, age, sex, CRP concentration, and antibiotic modification remained independently associated with guideline non-adherence. Each 10 mg/L increase in CRP was associated with a 23% increase in the odds of non-adherence. Female sex was associated with more than twofold higher adjusted odds of non-adherence, whereas antibiotic modification during treatment was associated with more than threefold higher adjusted odds of non-adherence. Increasing age showed an inverse association. The model demonstrated good discriminative ability (AUC = 0.824). The Firth penalized multivariable logistic regression analysis of factors independently associated with an unfavorable clinical outcome is presented in Table 10.

Table 10. Firth penalized multivariable logistic regression analysis of factors associated with an unfavorable clinical outcome.

Factor	AOR	95% CI	*p*-Value
Male sex	4.37	1.84–11.40	0.001
CRP, per 10 mg/L increase	1.22	1.09–1.37	<0.001
Intravenous administration	3.06	1.29–7.63	0.011
Guideline non-adherence	3.12	1.16–8.23	0.025

In the Firth penalized multivariable model, male sex, higher CRP concentration, intravenous administration, and guideline non-adherence remained independently associated with an unfavorable clinical outcome. Each 10 mg/L increase in CRP was associated with a 22% increase in the adjusted odds of an unfavorable clinical outcome. Male sex was associated with more than fourfold higher adjusted odds, while intravenous administration and guideline non-adherence were each associated with approximately threefold higher adjusted odds of an unfavorable clinical outcome. The model showed good discrimination for the clinical outcome (AUC = 0.864).

4. Discussion

The present study provided a comprehensive assessment of systemic antibiotic pharmacotherapy, adherence to clinical guidelines, and treatment outcomes among patients with bacterial skin infections managed in a dermatology department. Overall, 89.7% of patients received systemic pharmacotherapy consistent with the predefined guideline-based framework, while 88.7% achieved a favorable clinical outcome. Despite these generally favorable findings, guideline non-adherence remained independently associated with unfavorable clinical outcomes, while several clinical and pharmacotherapeutic characteristics were associated with prescribing adherence and treatment response. These findings provide real-world evidence relevant to antimicrobial stewardship and the optimization of systemic antibiotic use in dermatological practice.

4.1. Guideline Adherence and Associated Factors

The guideline-adherence rate of 89.7% observed in the present study was relatively high compared with rates reported in previous studies of antibiotic prescribing for skin and soft-tissue infections. In a nonrandomized controlled trial evaluating a multifaceted antimicrobial stewardship intervention, guideline adherence increased from 41% before implementation to 51% during the intervention period, while antibiotic treatment duration decreased by 26% [11]. Substantial gaps between guideline recommendations and real-world management have also been documented. In an emergency department study evaluating adherence to IDSA recommendations, overall management was fully guideline-concordant in only 20.1% of cases, with non-recommended antibiotics frequently initiated for both non-purulent and purulent infections [12]. More recent evidence has shown that reductions in broad-spectrum antibiotic use and treatment duration can be maintained for up to 12 years following implementation of a local treatment guideline, supporting institution-specific guidance as a sustainable stewardship strategy [13]. The higher adherence observed in our cohort may reflect differences in patient characteristics, dermatological case mix, prescribing practices, and the diagnosis-specific framework used to evaluate treatment appropriateness. Direct comparisons should therefore be interpreted cautiously because definitions of adherence and clinical settings differ among studies.

Higher CRP concentrations were independently associated with guideline non-adherence, with a 23% increase in the adjusted odds of non-adherence for every 10 mg/L

increase in CRP. This association should not be interpreted as evidence that elevated CRP directly caused inappropriate prescribing. Rather, CRP may represent greater inflammatory burden and potentially more clinically complex infection, thereby increasing the complexity of guideline-based therapeutic decision-making. In patients hospitalized with cellulitis, higher pretreatment CRP levels have been independently associated with longer durations of intravenous antibiotic therapy, suggesting that inflammatory burden may provide complementary information when treatment plans are formulated [14].

Antibiotic modification occurred in 17.3% of patients and was independently associated with guideline non-adherence, with more than threefold higher adjusted odds among patients whose regimen was modified. Treatment modification may occur because of inadequate initial response, microbiological findings, suspected resistance, intolerance, or reassessment of diagnosis or severity and should therefore not itself be interpreted as inappropriate practice. Instead, this association may identify more complex treatment episodes in which the initial regimen was less likely to remain consistent with the predefined therapeutic framework. Antibiotic modification may consequently represent a useful marker for prospective antimicrobial stewardship review.

Younger age was independently associated with guideline non-adherence, while female sex was associated with higher adjusted odds of non-adherence. Conversely, male sex was independently associated with an unfavorable clinical outcome. The contrasting sex-related associations may reflect differences in infection distribution and anatomical localization, severity at presentation, comorbidity patterns, healthcare-seeking behavior, or treatment-related characteristics. Behavioral factors influencing the timing of presentation or adherence to treatment recommendations may also have contributed. However, these mechanisms were not specifically evaluated and remain explanatory hypotheses rather than demonstrated causal pathways. Residual confounding by unmeasured clinical or behavioral characteristics cannot be excluded. These findings should therefore be regarded primarily as signals for further investigation rather than evidence of intrinsic biological differences in prescribing appropriateness or treatment response. Larger multicenter studies with more detailed adjustment for disease severity, anatomical distribution, behavioral characteristics, and other patient-level factors are needed to clarify these relationships.

4.2. Pharmacotherapeutic Patterns, Microbiology, and Antimicrobial Stewardship

The pharmacotherapeutic profile provided insight into systemic antibiotic use in routine dermatological practice. Oral administration accounted for 70.0% of treatment episodes, intravenous therapy for 30.0%, and monotherapy was used in 83.3% of patients. Amoxicillin/clavulanate, cephalexin, and clindamycin were among the most frequently prescribed antibiotics. The diversity of agents was consistent with the heterogeneous diagnostic spectrum represented in the study. Importantly, prescribing recommendations are not completely uniform across guidelines, and comparative analyses of hospital guidance documents and regional standards have demonstrated substantial variability in recommended antibiotic classes for common infections, including cellulitis [15]. Assessment of prescribing quality should therefore incorporate diagnosis, severity, likely pathogens, microbiological information, route, dose, and duration rather than relying exclusively on the identity of the prescribed antibiotic.

Microbiological culture was performed in 69.0% of patients. *Staphylococcus aureus* was the predominant isolate, followed by *Streptococcus pyogenes*, while MRSA accounted for 8.2% of isolates among cultured patients and Gram-negative organisms were identified less frequently. The predominance of *S. aureus* and streptococci was consistent with their established role as major pathogens in bacterial skin and soft-tissue infections. These findings reinforce the importance of aligning empirical antibiotic selection with the expected

microbiological profile and using culture results, when clinically indicated and available, to refine subsequent therapy. Microbiological information may be particularly valuable when initial clinical response is inadequate, resistant organisms are suspected, or broader-spectrum treatment has initially been required.

From an antimicrobial stewardship perspective, the high overall level of adherence indicates that structured systemic antibiotic prescribing was achievable across a heterogeneous group of bacterial skin infections. Nevertheless, patients with elevated inflammatory markers, those requiring antibiotic modification, and those receiving intravenous therapy may represent groups in whom pharmacotherapeutic review is particularly valuable. Previous stewardship interventions in skin and soft-tissue infections have shown that multifaceted strategies incorporating guideline-based education, structured treatment algorithms, electronic order sets, and audit and feedback can improve guideline adherence and reduce antibiotic treatment duration [11]. Similar approaches may provide practical opportunities to further optimize systemic pharmacotherapy in dermatological services.

4.3. Factors Associated with Clinical Outcomes

Guideline adherence showed an important relationship with clinical outcome. In the additional analysis of the three-category clinical outcome, the distribution of complete recovery, clinical improvement, and no clinical change differed significantly according to guideline adherence (p = 0.004). Complete recovery was similar between adherent and non-adherent treatment episodes (43.5% vs. 45.2%), whereas no clinical change was substantially less frequent among patients receiving guideline-adherent pharmacotherapy (9.3% vs. 29.0%). This pattern suggests that the principal difference was concentrated in persistence of an unfavorable response rather than in complete recovery alone.

Consistent with this finding, multivariable analysis showed that guideline non-adherence was associated with approximately threefold higher adjusted odds of an unfavorable clinical outcome. Previous evidence has similarly supported an association between improved adherence to treatment recommendations and better outcomes in skin and soft-tissue infections. In a study involving 1360 patients with non-purulent skin and soft-tissue infections, implementation of an algorithm-based clinical guideline increased guideline adherence and was accompanied by significant reductions in treatment failure and hospital readmission [6]. Treatment failure declined from 26.8% to 16.5%, while readmission decreased from 22.3% to 12.7% following the intervention. These findings support the clinical relevance of structured antibiotic prescribing and are consistent with the association observed in our cohort. Nevertheless, because the present study was retrospective and observational, the association between non-adherence and unfavorable outcome should not be interpreted as establishing causality.

Higher CRP was also independently associated with unfavorable clinical outcome, with a 22% increase in adjusted odds for every 10 mg/L increase. As with its association with non-adherence, CRP is more appropriately interpreted as a marker of inflammatory burden and clinical complexity than as a direct determinant of treatment failure. This interpretation is consistent with evidence linking higher pretreatment CRP with more intensive antibiotic management in hospitalized patients with cellulitis [14].

Intravenous antibiotic administration was independently associated with approximately threefold higher adjusted odds of an unfavorable clinical outcome. This finding should not be interpreted as evidence that intravenous therapy itself resulted in poorer outcomes. In routine clinical practice, intravenous treatment is preferentially used in patients with more severe infection, greater systemic involvement, inability to receive oral therapy, or other features requiring intensive management. The observed association may therefore reflect confounding by indication, whereby the underlying severity prompting

intravenous treatment also increases the probability of an unfavorable outcome. This distinction is particularly important in observational pharmacoepidemiological studies in which treatment allocation is clinically determined rather than randomized. The finding nevertheless supports regular reassessment of patients receiving intravenous antibiotics and transition to oral therapy when clinically appropriate.

4.4. Pharmacoepidemiological and Clinical Implications

From a pharmacoepidemiological perspective, the study demonstrates the value of evaluating antibiotic use beyond prescription frequencies alone. Integrating antibiotic selection with dose, route, treatment duration, combination therapy, treatment modification, microbiological findings, guideline adherence, and clinical outcomes provides a more clinically informative assessment of real-world pharmacotherapy. This multidimensional approach is particularly relevant for bacterial skin infections because antibiotic prescribing recommendations may vary across institutional guidance documents and regional standards, including for common infections such as cellulitis [15]. Diagnosis-specific evidence-based prescribing frameworks, combined with local microbiological information and antimicrobial stewardship principles, may therefore provide a more meaningful assessment of treatment appropriateness than evaluation of individual antibiotics in isolation.

Clinically, the findings identify several situations in which closer pharmacotherapeutic review may be useful, particularly treatment episodes characterized by elevated inflammatory burden, antibiotic modification, intravenous administration, or deviation from guideline-based treatment. These characteristics should not be regarded as causal determinants of poor outcome but as potential indicators of greater treatment complexity. Their identification may help focus stewardship activities on patients and treatment episodes in which reassessment of antibiotic selection, route, duration, microbiological information, and clinical response could be most informative.

4.5. Strengths and Limitations

The present study had several strengths. It included a well-defined cohort of 300 patients treated within a dermatology department and incorporated demographic, clinical, laboratory, microbiological, and detailed pharmacotherapeutic information. Systemic antibiotic treatment was evaluated across multiple dimensions, including antibiotic selection, dose, route, treatment duration, monotherapy or combination therapy, and treatment modification. Both guideline adherence and clinical outcome were evaluated as predefined outcomes, while microbiological findings and inflammatory parameters strengthened the clinical interpretation of prescribing patterns. Several limitations should be considered. First, the retrospective design depended on the completeness and accuracy of routinely documented medical records and did not permit control over the collection of clinical variables. Second, the single-center setting may limit generalizability to other hospitals, healthcare systems, or patient populations. Third, residual confounding could not be excluded, particularly regarding infection severity and the clinical decision to administer intravenous antibiotics. Fourth, microbiological cultures were not performed in all patients, restricting pathogen-specific analyses to those with available testing. Fifth, guideline adherence was evaluated using a predefined diagnosis-specific evidence-based framework, and differences between international and local recommendations may have influenced classification of individual treatment regimens. Sixth, the relatively small numbers of guideline non-adherence events and unfavorable clinical outcomes limited the number of covariates that could be included in the multivariable models and may have reduced the precision of some estimates. Finally, the observational design permits identification of associations but does not establish causal relationships between pharmacotherapeutic characteristics,

guideline adherence, and clinical outcomes. Despite these limitations, the study provides real-world evidence on systemic antibiotic pharmacotherapy in dermatological practice and identifies clinically relevant factors associated with prescribing adherence and treatment outcomes. The findings support continued integration of diagnosis-specific treatment guidance, microbiological assessment when clinically indicated, and antimicrobial stewardship principles into the management of bacterial skin infections.

5. Conclusions

This study provided a comprehensive evaluation of systemic antibiotic pharmacotherapy for bacterial skin infections in routine dermatological practice. Overall, adherence to clinical guidelines was high, with 89.7% of treatment regimens classified as guideline-adherent, while 88.7% of patients achieved a favorable clinical outcome. Nevertheless, a clinically relevant proportion of patients received non-adherent pharmacotherapy or experienced an unfavorable treatment outcome. Higher CRP concentrations were independently associated with both guideline non-adherence and unfavorable clinical outcomes, while antibiotic modification during treatment was independently associated with non-adherence. Intravenous antibiotic administration was independently associated with an unfavorable clinical outcome, although this association should be interpreted in the context of potential confounding by indication and greater underlying infection severity. Most importantly, guideline non-adherence was independently associated with approximately threefold higher adjusted odds of an unfavorable clinical outcome. These findings emphasize the clinical and pharmacoepidemiological importance of appropriate systemic antibiotic selection and structured assessment of dose, route of administration, treatment duration, and treatment modification in patients with bacterial skin infections. Continued implementation of diagnosis-specific, evidence-based prescribing principles, supported by microbiological and clinical assessment when appropriate, may contribute to optimizing systemic pharmacotherapy and strengthening antimicrobial stewardship in dermatological practice. Given the single-center nature of this study, the findings should be interpreted within the context of the local clinical setting and may not be fully generalizable to other healthcare institutions or patient populations. Future prospective and multicenter studies are warranted to confirm these associations and evaluate their generalizability across different clinical settings.

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