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Empirical Antibiotic Use Patterns in Patients With Sepsis: A Cross-Sectional Study

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Abstract

Background and objectives: Sepsis-related morbidity and mortality increase when appropriate empirical antibiotic therapy is not administered. Changes in antimicrobial susceptibility patterns reflect the emergence of multidrug-resistant organisms. These global concerns can be addressed through the judicious use of empirical antibiotics. Therefore, we conducted this study to determine the usage patterns of empirical antibiotics in patients with sepsis arising from various suspected sources of infection. Additionally, we examined the associations between empirical antibiotic use and the detected pathogens.

Materials and methods: This cross-sectional study was conducted at Kalinga Institute of Medical Sciences (KIMS), Bhubaneswar, India, from October 2025 to September 2026. We enrolled adult patients with sepsis admitted to the KIMS medical intensive care unit during the study period. We recorded Sequential Organ Failure Assessment (SOFA) scores and white blood cell (WBC) counts. The associations between empirical antibiotics and pathogenic bacteria were illustrated using alluvial plots. We analyzed the collected data by suspected source of infection (i.e., abdomen, central nervous system (CNS), respiratory system, skin and soft tissue, and urinary system). R software version 4.6.1 (R Core Team, Vienna, Austria) was employed for data analysis.

Results: We analyzed data from 683 patients with sepsis (median age: 58.0 years; males: 384 (56.22%)). The median length of hospital stay was 17.0 (14.0-21.0) days. The most common suspected source of infection was the respiratory system (276, 40.41%), followed by the urinary system (191, 27.96%), abdomen (96, 14.06%), CNS (74, 10.83%), and skin and soft tissue (46, 6.73%). On day 0, the median SOFA scores of the participants with abdominal, CNS, respiratory, skin and soft tissue, and urinary infections were 5.0 (3.0-6.0), 4.0 (3.0-7.5), 5.0 (3.0-6.0), 5.0 (2.0-8.8), and 4.0 (3.0-6.0), respectively (p = 0.850). The corresponding WBC counts were 17.2 (14.8-19.3) × 10^9/L, 16.3 (14.8-19.0) × 10^9/L, 16.8 (14.6-19.2) × 10^9/L, 16.3 (14.7-19.1) × 10^9/L, and 17.1 (14.8-19.2) × 10^9/L, respectively (p = 0.802). Regardless of the source of infection, beta-lactams were the mainstay of empirical antimicrobial therapy. Ceftriaxone, meropenem, and piperacillin-tazobactam were the most commonly used empirical antibiotics in our study population. The most common pathogenic bacteria detected among participants with abdominal, CNS, respiratory, skin and soft tissue, and urinary infections were *Escherichia coli* (25/96, 26.0%), *Streptococcus pneumoniae* (19/74, 25.7%), *Klebsiella pneumoniae* (92/276, 33.3%), *Streptococcus pyogenes* (12, 26.1%), and *Escherichia coli* (72, 37.7%), respectively. Most combination therapies remained unchanged following the culture and antimicrobial susceptibility testing results.

Conclusions: Beta-lactams were the most commonly used class of antibiotics for empirical therapy in our study population. Respiratory and urinary infections were more common than other infections. *Escherichia coli* and *Klebsiella pneumoniae* were the most common pathogenic bacteria detected among participants.

Categories: Family/General Practice, Epidemiology/Public Health, Infectious Disease
Keywords: alluvial plot, antimicrobial resistance, broad-spectrum antibiotics, culture and sensitivity, empirical antibiotic therapy, prolonged hospitalization, sepsis treatment, severe bacterial infection, sofa score, white blood cell count (wbc)

Introduction

A dysregulated response to infection leads to sepsis. Its most common consequences are systemic inflammation and multiple organ failure [1,2]. The sepsis-related mortality rate in India is around 28-36% according to recent studies [3,4]. In low- and middle-income countries such as India, sepsis hinders economic growth by aggravating sepsis-related morbidity and mortality [3-5]. Antibiotic therapy is regarded as the most effective management for patients with sepsis [6]. Early administration of antibiotic therapy increases the chance of survival in patients with bacteremia [6,7]. Generally, antibiotic therapy is selected empirically when managing patients with sepsis [6]. Empirical antibiotics are crucial because the causative pathogen or its antimicrobial susceptibility patterns are unknown [6,8]. The Sepsis-3 criteria define sepsis as life-threatening organ dysfunction caused by a dysregulated host response to infection [9]. The Sequential

Organ Failure Assessment (SOFA) score is used to assess sepsis severity [10].

Appropriate samples are sent for pathogen identification and antimicrobial susceptibility testing (AST) before antibiotic therapy is initiated [11]. Pathogenic microbes trigger sepsis by causing bloodstream infections (BSIs), catheter-related BSIs (CRBSIs), or organ-specific infections [12]. The antimicrobial susceptibility patterns of common hospital pathogens causing specific infections change over time [13,14]. In these settings, choosing empirical antibiotic therapy is challenging because of its impact on health outcomes and hospital burden [3,6,15]. Timely recognition of the most likely source of infection is key to selecting appropriate empirical antimicrobial therapy [15,16]. Clinical symptoms, experience, and knowledge of common pathogens associated with the suspected infection, their antimicrobial susceptibility patterns, and the appropriateness of antibiotics help determine the patient's outcome [15]. The site of infection plays a significant role in predicting pathogens, selecting appropriate microbiological samples, and guiding subsequent multidisciplinary approaches [15,16]. Furthermore, the diagnostic procedures and their timing depend on source identification and the initiation of appropriate empirical antimicrobial therapy [15]. Because antibiotics differ in tissue penetration, mechanisms of action, tissue specificity, half-lives, and other pharmacokinetic-pharmacodynamic (PK-PD) parameters, the source of infection helps guide antibiotic selection [15,17,18].

Most hospital-acquired infections are caused by *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* species [19]. These ESKAPE pathogens can thrive in most hospital environments owing to their resistance determinants [19]. As pathogens enter the body, the inflammatory and immune responses are mediated by neutrophils, macrophages, B cells, and T cells [20]. Pattern recognition receptors (PRRs) on immune cells recognize pathogen-associated molecular patterns [20-22]. PRRs then stimulate innate immune activation and the upregulation of inflammatory genes to combat pathogens and maintain immune homeostasis [20,21]. Nevertheless, resistant pathogens evade host immune defenses and disrupt immune homeostasis, causing tissue damage, organ dysfunction, and sepsis [20-23].

Sepsis is most commonly evaluated using the SOFA score [10]. White blood cell (WBC) count, neutrophil-to-lymphocyte ratio, and systemic immune-inflammation index also serve as sepsis biomarkers [24]. Appropriate empirical antimicrobial therapy and the absence of multidrug-resistant organisms (MDROs) in culture reports are two key factors that improve patient outcomes and reduce hospital burden [15]. The presence of MDROs in the reports necessitates either replacing ongoing empirical antimicrobial therapy or adding other antibiotics. This change can lead to drug interactions, reduced host response, and prolonged hospitalization [17].

We conducted this study to determine the usage patterns of empirical antibiotics in patients with sepsis arising from various suspected sources of infection. We also evaluated the WBC counts and SOFA scores of the study participants. Additionally, we assessed the associations between empirical antibiotic use and the pathogens detected by culture and sensitivity testing.

Materials And Methods

We conducted this cross-sectional study from October 2025 to September 2026 at Kalinga Institute of Medical Sciences (KIMS), Bhubaneswar, India. We obtained ethical approval from the Institutional Ethics Committee (approval number: KIIT/KIMS/IEC/2307/2025, approval date: September 22, 2025) before enrolling any participant.

Study criteria

Adult patients admitted to the medical intensive care unit (ICU) during the study period who met the Sepsis-3 criteria were screened for this study [9]. We excluded patients who had sepsis before ICU admission, were referred from other hospitals, or had received any antibiotics within the preceding seven days. Patients who stayed for less than seven days or died within seven days were also excluded. Patients who met the eligibility criteria were enrolled.

Study objectives

We conducted this study to determine the usage patterns of various empirical antibiotics among patients with sepsis admitted to our hospital's ICU. This study analyzed data from patients with sepsis arising from various suspected sources of infection (i.e., abdomen, central nervous system (CNS), respiratory system, skin and soft tissue, and urinary system). We assessed the length of hospital stay, empirical antibiotic use, and pathogenic bacteria identified by culture and sensitivity testing. We evaluated sepsis progression using SOFA scores and WBC counts. We also assessed whether empirical antibiotics were altered after culture and sensitivity testing. All these parameters were further evaluated according to the suspected sources of infection.

Study procedure

At enrollment, we collected participants' demographic and clinical characteristics. These included age, gender, body mass index (BMI), comorbidities such as type 2 diabetes mellitus (T2DM) and hypertension, and a history of ICU admission or hospitalization for any infection. We assessed these parameters based on the source of infection. In this study, those aged 65 years or older were regarded as "elderly," and those aged 18 to 65 years were considered adults. We asked the participants or their close relatives about the presence of comorbidities such as T2DM and hypertension and a history of ICU admission or hospitalization for any infection.

Sepsis Evaluation

All participants were assessed using the Sepsis-3 criteria [9] to diagnose sepsis. Sepsis is indicated by an abrupt increase of >2 in the SOFA score from baseline in patients with any known or suspected infection. The SOFA score evaluates six parameters across different organ systems (i.e., CNS, respiratory, cardiovascular, hepatic, renal, and coagulation) [10]. CNS function is assessed using the Glasgow Coma Scale. Respiratory status is evaluated using the ratio of arterial oxygen partial pressure to the fraction of inspired oxygen. Cardiovascular function is assessed using mean arterial pressure. Hepatic function is reflected by the serum bilirubin level. Renal function is measured using serum creatinine. Coagulation function is assessed using the platelet count. Each of these six parameters is scored from 0 to 4, where 0 indicates normal function and 4 indicates severe dysfunction or failure. This gives the SOFA score a range of 0 to 24. Higher SOFA scores indicate greater sepsis severity and a poorer prognosis [10]. In our hospital, all patients with sepsis are routinely monitored with the SOFA score. In this study, we considered the day of enrollment as day 0. The SOFA scores for all participants were reassessed on days 3 and 7. WBC counts were also evaluated on days 0, 3, and 7.

Sample Collection, Empirical Antibiotics, and Culture Reports

Because our study population was heterogeneous, the types of samples collected varied among participants. Sputum, bronchoalveolar lavage, and/or endotracheal tube aspirates were obtained from participants with suspected respiratory infections. Cerebrospinal fluid was collected from those with suspected CNS infection. Urine and blood samples were obtained from those with suspected urinary infections. Tissue, blood, and pus samples were collected from participants with suspected abdominal infections or skin and soft tissue infections. Blood samples were collected from each participant to assess for BSI or CRBSI. Samples were obtained from all participants under aseptic conditions before empirical antibiotic therapy was initiated. Owing to the non-interventional design, none of the study investigators were involved in selecting empirical antibiotics or determining their dosing schedules for any study participant. The choice of empirical antibiotics was entirely at the clinicians' discretion. All samples were immediately sent to the microbiology laboratory for culture and sensitivity. The VITEK 2 system (BioMérieux, Marcy-l'Étoile, France) was used to identify the pathogenic bacteria and perform AST on the isolates. The AST results were assessed using the 2024 cutoff values set by the Clinical and Laboratory Standards Institute (CLSI) [25]. The same clinicians who selected the empirical antibiotics also decided whether to change the antibiotics, modify their dosing schedules, continue the existing therapy, or add another antibiotic. We defined "change" as any change in the dosing frequency or dose of the empirical antibiotics, in accordance with the culture reports and AST results. We classified participants who either continued the same empirical antibiotic without modification of the dosing schedule or added other antibiotics without changing the dosing schedule of the ongoing empirical antibiotic as having no change in empirical antibiotic therapy. We also recorded the length of hospital stay from the medical records. All findings were assessed according to different sources of infection.

Statistical analysis

For this cross-sectional study, we adopted nonprobability consecutive sampling. The Shapiro-Wilk test assessed the normality of the data distribution. Continuous data were presented as medians and interquartile ranges (IQRs). The categorical data were presented as frequencies and proportions. Continuous and categorical data were assessed using the Kruskal-Wallis test and the chi-square test, respectively. We also computed the corresponding H values and chi-square values. For the post hoc analysis, we used the Bonferroni correction. We generated a Voronoi treemap to illustrate the distribution of the study participants. Alluvial plots were generated to illustrate the associations between empirical antibiotic use and gender, age group, detected pathogenic bacteria, drug changes per the culture and sensitivity report, and participants' duration of hospitalization. R software version 4.6.1 (R Core Team, Vienna, Austria) was used for data analysis and plot generation [26]. Statistical significance was set at $p < 0.05$.

Results

During the study period, 1,471 patients in the medical ICU were diagnosed with sepsis. Of these, 237 (16.11%) were referred from other hospitals and were on antibiotics. A total of 462 (31.41%) patients were transferred to the ICU for sepsis management. Empirical antibiotics were started in 28 (1.90%) patients before samples were sent for culture and sensitivity testing. A total of 61 (4.15%) patients either died or left against medical advice within seven days. Data from the remaining 683 (46.43%) patients were analyzed in this study. Table *1* shows the demographic and clinical characteristics of the 683 participants. The median age was 58.0 (47.0-63.0) years. Approximately one-fifth (137, 20.06%) of the participants were aged over 65

years. Among the participants, 384 (56.22%) were male. T2DM and hypertension were observed in 293 (42.90%) and 131 (19.18%) participants, respectively. In the study population (n = 683), the most common suspected source of infection was the respiratory system (276, 40.41%), followed by the urinary system (191, 27.96%), abdomen (96, 14.06%), CNS (74, 10.83%), and skin and soft tissue (46, 6.73%). All 46 participants with skin and soft tissue infection had T2DM. The proportions of older adults among participants with CNS (29, 39.19%) and skin and soft tissue infections (11, 23.91%) were higher than those among participants with other infections ($p < 0.001$). A total of 135 (19.77%) participants had previously been hospitalized for infections. A total of 47 (6.88%) participants had a history of ICU admission.

Parameters	Total participants (n = 683)	Participants with abdominal infection (n = 96)	Participants with CNS infection (n = 74)	Participants with respiratory infection (n = 276)	Participants with skin and soft tissue infection (n = 46)	Participants with urinary infection (n = 191)	Statistical test used	Test statistics	p-value
Age (years)	58.0 (47.0-63.0)	57.0 (46.0-62.0)	60.0 (55.0-70.0)	57.0 (44.0-63.0)	59.5 (55.0-63.0)	57.0 (53.0-63.0)	Kruskal-Wallis test	13.24	0.010
Age >65 years	137 (20.06%)	16 (16.67%)	29 (39.19%)	51 (18.48%)	11 (23.91%)	30 (15.71%)	Chi-square test	20.69	< 0.001
Male gender	384 (56.22%)	58 (60.42%)	42 (56.76%)	151 (54.71%)	27 (58.70%)	106 (55.50%)	Chi-square test	1.11	0.893
BMI (kg/m^2)	26.30 (24.35-27.40)	26.15 (24.38-27.40)	26.55 (24.55-27.50)	25.70 (24.0-27.10)	26.55 (24.85-27.28)	26.60 (24.40-27.80)	Kruskal-Wallis test	8.69	0.070
Comorbidity									
T2DM	293 (42.90%)	44 (45.83%)	38 (51.35%)	98 (35.51%)	46 (100.00%)	67 (35.08%)	Chi-square test	74.65	< 0.001
Hypertension	131 (19.18%)	16 (16.67%)	18 (24.32%)	52 (18.84%)	13 (28.26%)	32 (16.75%)	Chi-square test	4.85	0.303
Duration of hospitalization (days)	17.0 (14.0-21.0)	17.0 (15.0-22.0)	17.0 (13.3-20.0)	17.0 (14.0-22.0)	15.0 (13.0-18.0)	17.0 (14.0-21.5)	Kruskal-Wallis test	5.02	0.290
History of ICU admission	47 (6.88%)	8 (8.33%)	6 (8.11%)	16 (5.80%)	5 (10.87%)	12 (6.28%)	Chi-square test	2.24	0.691
History of hospitalization due to any infection	135 (19.77%)	23 (23.96%)	16 (21.62%)	50 (18.12%)	8 (17.39%)	38 (19.90%)	Chi-square test	1.86	0.761

TABLE 1: Demographic and clinical details of the study participants (n = 683)

The categorical data were presented as frequencies and proportions. The continuous data were presented as medians and IQRs. Categorical and continuous data were analyzed using the chi-square ($\chi 2$) test and the Kruskal-Wallis test, respectively. The chi-square values for the chi-square test, H values for the Kruskal-Wallis test, and p-values were calculated. A p-value < 0.05 was regarded as statistically significant.

BMI: body mass index, T2DM: type 2 diabetes mellitus, CNS: central nervous system, ICU: intensive care unit, IQR: interquartile range

The Voronoi treemap in Figure *1* demonstrates the study population's distribution.

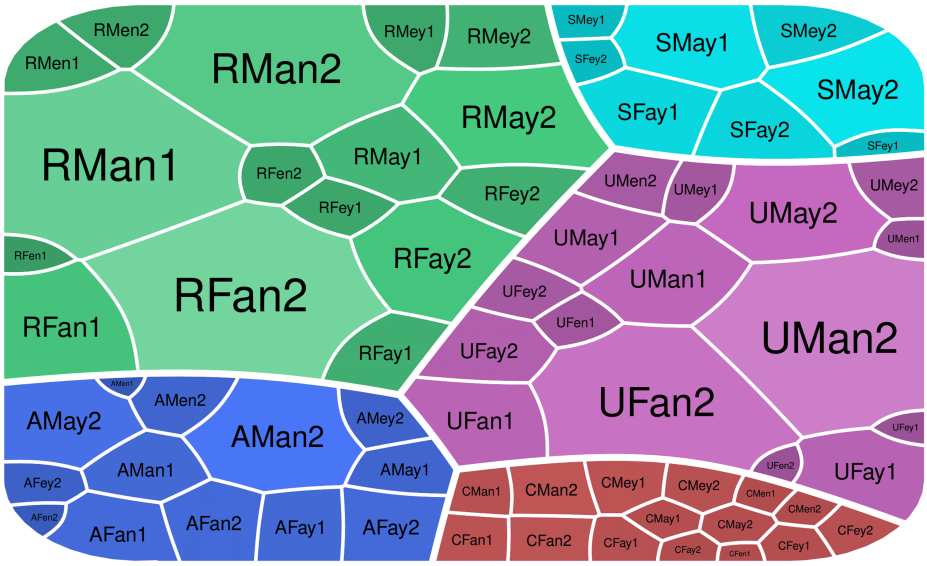


FIGURE 1: Distribution of the study participants

The five colors (steel blue, coral red, sea green, cyan, and orchid) indicate the suspected sources of infection (abdomen, CNS, respiratory system, skin and soft tissue, and urinary system) in the participants. The dimension of each block is proportional to the number of participants in that block. Each block has a distinct name containing five alphanumeric characters. The first character denotes the source of infection (A: abdomen, C: CNS, R: respiratory system, S: skin and soft tissue, or U: urinary system). The second character denotes the participants' gender (M: male, F: female). The third and fourth characters denote their age group (a: adult or e: elderly) and presence of T2DM (y: yes, or n: no), respectively. The fifth character indicates whether antibiotics were given empirically (1 or 2). Fifty-three (7.76%) adult non-diabetic female participants with respiratory infections received two empirical antibiotics (RFan2 in the plot). Forty-eight (7.03%) adult non-diabetic male participants with respiratory infections received one empirical antibiotic (RMan1 in the plot). Forty-four (6.44%) adult non-diabetic male subjects with urinary infections received two empirical antibiotics (UMan2 in the plot). Forty-one (6.00%) adult non-diabetic male participants with respiratory infections received two empirical antibiotics (RMan2 in the plot). Thirty-eight (5.56%) adult non-diabetic female participants with urinary infections received two empirical antibiotics (UFan2 in the plot). Twenty-three (3.37%) adult male diabetic subjects with respiratory infections received two empirical antibiotics (RMay2 in the plot). All 46 participants with skin and soft tissue infection had T2DM.

CNS: central nervous system, T2DM: type 2 diabetes mellitus

This plot was generated using R software version 4.6.1 (R Core Team, Vienna, Austria) [26].

Age, BMI, and duration of hospitalization

The age distribution is shown in Figure *2*. The median age of the study participants was 58.0 (47.0-63.0) years. The median ages of participants with abdominal, CNS, respiratory, skin and soft tissue, and urinary infections were 57.0 (46.0-62.0) years, 60.0 (55.0-70.0) years, 57.0 (44.0-63.0) years, 59.5 (55.0-63.0) years, and 57.0 (53.0-63.0) years, respectively (p = 0.010). The post hoc analysis with Bonferroni correction revealed a statistically significant difference in age between participants with CNS infections and those with respiratory infections. The remaining intergroup differences were not statistically significant. Table *1* also presents the age distribution.

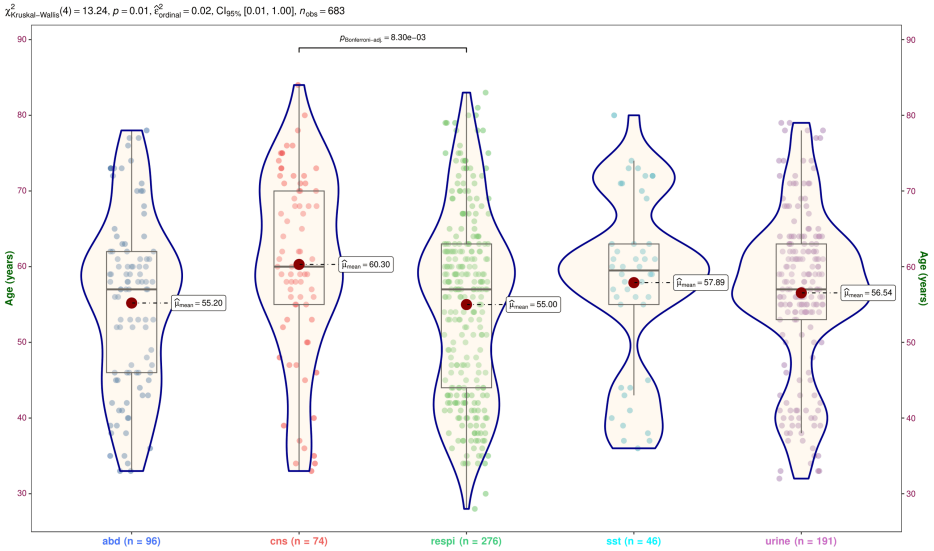


FIGURE 2: Age of the study participants

The box-and-whisker, jitter, and violin plots demonstrate the age distribution of the study participants (n = 683). The mean values are shown as red dots. For analysis, we used the Kruskal-Wallis test and Bonferroni correction. A p-value < 0.05 was regarded as statistically significant. Only the significant intergroup differences are shown.

abd: abdomen, cns: central nervous system, respi: respiratory system, sst: skin and soft tissue, urine: urinary system

This plot was generated using R software version 4.6.1 (R Core Team, Vienna, Austria) [26].

The participants' BMI is shown in Figure *3*. The median BMI of the study participants was 26.30 (24.35-27.40) kg/m². The median BMIs of participants with abdominal, CNS, respiratory, skin and soft tissue, and urinary infections were 26.15 (24.38-27.40) kg/m², 26.55 (24.55-27.50) kg/m², 25.70 (24.0-27.10) kg/m², 26.55 (24.85-27.28) kg/m², and 26.60 (24.40-27.80) kg/m², respectively (p = 0.070). The post hoc analysis with Bonferroni correction revealed no statistically significant intergroup differences. Table *1* also presents the participants' BMI.

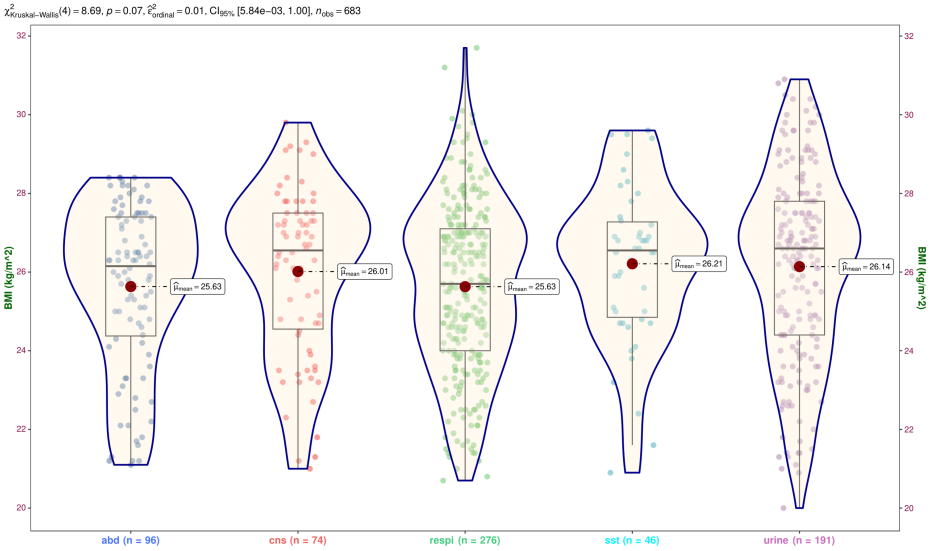


FIGURE 3: BMI of the study participants

The box-and-whisker, jitter, and violin plots demonstrate the BMI of the study participants (n = 683). The mean values are shown as red dots. For analysis, we used the Kruskal-Wallis test and Bonferroni correction. A p-value < 0.05 was regarded as statistically significant. Only the significant intergroup differences are shown.

BMI: body mass index, abd: abdomen, CNS: central nervous system, respi: respiratory system, sst: skin and soft tissue, urine: urinary system

This plot was generated using R software version 4.6.1 (R Core Team, Vienna, Austria) [26].

The length of hospital stay among the study participants is shown in Figure *4*. The median length of hospital stay among the study participants was 17.0 (14.0-21.0) days. The median lengths of hospital stay among participants with abdominal, CNS, respiratory, skin and soft tissue, and urinary infections were 17.0 (15.0-22.0) days, 17.0 (13.3-20.0) days, 17.0 (14.0-22.0) days, 15.0 (13.0-18.0) days, and 17.0 (14.0-21.5) days, respectively (p = 0.290). The post hoc analysis using the Bonferroni correction revealed that none of the intergroup differences were statistically significant. Table *1* also presents the lengths of hospital stay among the study participants.

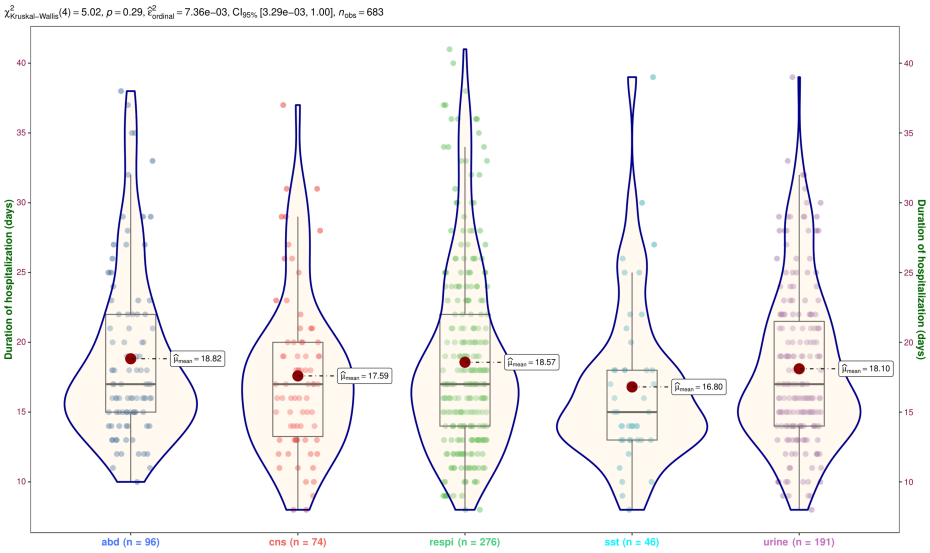


FIGURE 4: Duration of hospitalization of the study participants

The box-and-whisker, jitter, and violin plots show the length of hospital stay of the study participants (n = 683). The mean values are shown as red dots. For analysis, we used the Kruskal-Wallis test and Bonferroni correction. A p-value < 0.05 was regarded as statistically significant. Only the significant intergroup differences are shown.

abd: abdomen, cns: central nervous system, respi: respiratory system, sst: skin and soft tissue, urine: urinary system

This plot was generated using R software version 4.6.1 (R Core Team, Vienna, Austria) [26].

SOFA score and WBC count

Figure *5* and Table *2* demonstrate the SOFA scores of the study participants. On day 0, the median SOFA scores of the participants with abdominal, CNS, respiratory, skin and soft tissue, and urinary infections were 5.0 (3.0-6.0), 4.0 (3.0-7.5), 5.0 (3.0-6.0), 5.0 (2.0-8.8), and 4.0 (3.0-6.0), respectively (p = 0.850). On day 3, the corresponding SOFA scores were 5.0 (3.0-6.0), 5.0 (2.3-7.0), 5.0 (2.8-8.0), 6.0 (3.0-8.0), and 5.0 (3.0-6.0), respectively (p = 0.310). On day 7, the corresponding SOFA scores were 4.0 (2.0-6.0), 4.0 (2.0-7.8), 4.0 (2.0-7.0), 6.0 (2.3-8.0), and 4.0 (2.0-7.0), respectively (p = 0.210).

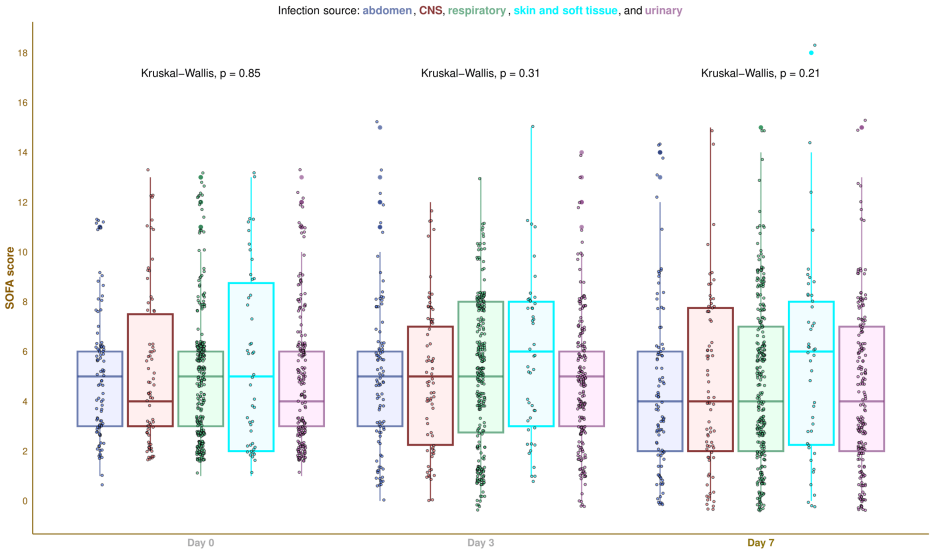


FIGURE 5: SOFA scores of the study participants

The box-and-whisker plots illustrate the SOFA scores of the study population on days 0, 3, and 7. The data were analyzed with the Kruskal-Wallis test. A p-value < 0.05 was regarded as statistically significant.

SOFA: Sequential Organ Failure Assessment, CNS: central nervous system

This plot was generated using R software version 4.6.1 (R Core Team, Vienna, Austria) [26].

Parameters	Time point of assessment	Total participants (n = 683)	Participants with abdominal infection (n = 96)	Participants with CNS infection (n = 74)	Participants with respiratory infection (n = 276)	Participants with skin and soft tissue infection (n = 46)	Participants with urinary infection (n = 191)	Test statistics	p-value
SOFA score	Day 0	5.0 (3.0-6.0)	5.0 (3.0-6.0)	4.0 (3.0-7.5)	5.0 (3.0-6.0)	5.0 (2.0-8.8)	4.0 (3.0-6.0)	1.34	0.850
	Day 3	5.0 (2.0-7.0)	5.0 (3.0-6.0)	5.0 (2.3-7.0)	5.0 (2.8-8.0)	6.0 (3.0-8.0)	5.0 (3.0-6.0)	4.76	0.310
	Day 7	4.0 (2.0-7.0)	4.0 (2.0-6.0)	4.0 (2.0-7.8)	4.0 (2.0-7.0)	6.0 (2.3-8.0)	4.0 (2.0-7.0)	5.81	0.210
WBC count (10^9/L)	Day 0	16.95 (14.70-19.20)	17.2 (14.8-19.3)	16.3 (14.8-19.0)	16.8 (14.6-19.2)	16.3 (14.7-19.1)	17.1 (14.8-19.2)	1.64	0.802
	Day 3	15.80 (14.10-17.90)	16.2 (14.8-19.0)	15.4 (13.9-17.0)	15.8 (14.2-17.9)	15.8 (14.2-18.5)	15.8 (13.9-17.8)	8.28	0.082
	Day 7	14.61 (12.60-16.80)	16.0 (13.5-17.3)	13.9 (12.2-16.5)	14.6 (12.7-16.6)	15.0 (12.5-17.8)	14.3 (12.4-16.4)	14.29	0.006

TABLE 2: SOFA score and WBC count of the study participants (n = 683)

The continuous data were presented as medians and IQRs. We analyzed these data using the Kruskal-Wallis test and calculated H values. A p-value < 0.05 was regarded as statistically significant.

SOFA: Sequential Organ Failure Assessment, WBC: white blood cell, IQR: interquartile range

Figure *6* and Table *2* demonstrate the WBC counts of the study participants. On day 0, the median WBC counts of the participants with abdominal, CNS, respiratory, skin and soft tissue, and urinary infections were 17.2 (14.8-19.3) × 10^9/L, 16.3 (14.8-19.0) × 10^9/L, 16.8 (14.6-19.2) × 10^9/L, 16.3 (14.7-19.1) × 10^9/L, and 17.1 (14.8-19.2) × 10^9/L, respectively (p = 0.802). On day 3, the corresponding WBC counts were 16.2 (14.8-19.0) × 10^9/L, 15.4 (13.9-17.0) × 10^9/L, 15.8 (14.2-17.9) × 10^9/L, 15.8 (14.2-18.5) × 10^9/L, and 15.8 (13.9-17.8) × 10^9/L, respectively (p = 0.082). On day 7, the corresponding WBC counts were 16.0 (13.5-17.3) × 10^9/L, 13.9

(12.2-16.5) × 10^9/L, 14.6 (12.7-16.6) × 10^9/L, 15.0 (12.5-17.8) × 10^9/L, and 14.3 (12.4-16.4) × 10^9/L, respectively (p = 0.006).

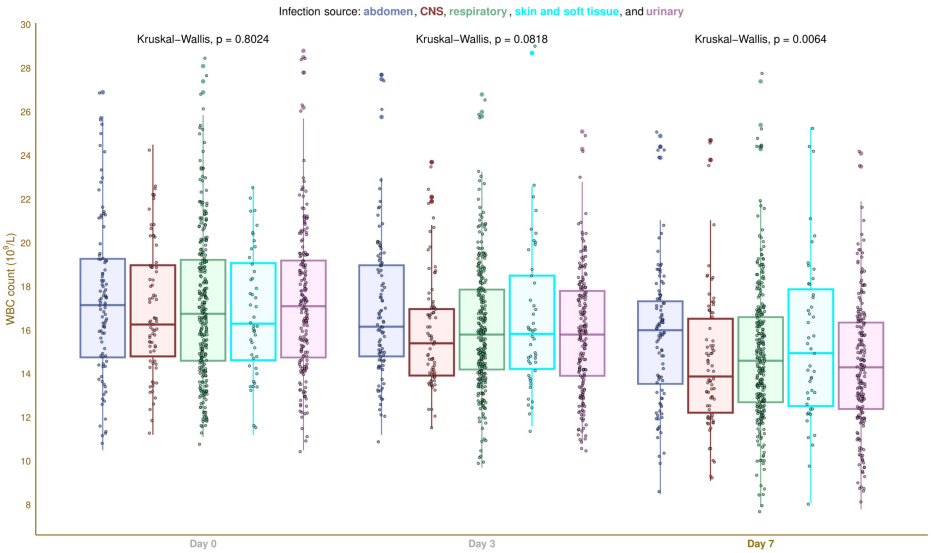


FIGURE 6: WBC counts of the study participants

The box-and-whisker plots illustrate the WBC counts of the study population on days 0, 3, and 7. The data were analyzed with the Kruskal-Wallis test. A p-value < 0.05 was regarded as statistically significant.

WBC: white blood cell, CNS: central nervous system

This plot was generated using R software version 4.6.1 (R Core Team, Vienna, Austria) [26].

Usage patterns of empirical antibiotics

The alluvial plot in Figure 7 shows the associations between empirical antibiotic use and gender, age group, detected pathogenic bacteria, changes in drugs per the culture and sensitivity report, and length of hospital stay among participants with suspected abdominal infection. Of the 96 participants with suspected abdominal infections, 46 (47.9%) were adult males and 34 (35.4%) were adult females. The most commonly prescribed empirical antibiotic therapy was a combination of meropenem and cotrimoxazole (25, 26.0%). The most commonly detected pathogenic bacterium was *Escherichia coli* (25, 26.0%), followed by *Klebsiella pneumoniae* (19, 19.8%) and *Pseudomonas aeruginosa* (16, 16.7%). The empirical antibiotic therapy of 57 (59.4%) participants remained unchanged after the culture and AST results were received. Neither the combination of cotrimoxazole and meropenem (25, 26.0%) nor that of cotrimoxazole and ceftazidime (6, 6.3%) was replaced. All empirical monotherapies (31, 32.3%) were modified based on the culture and AST results.

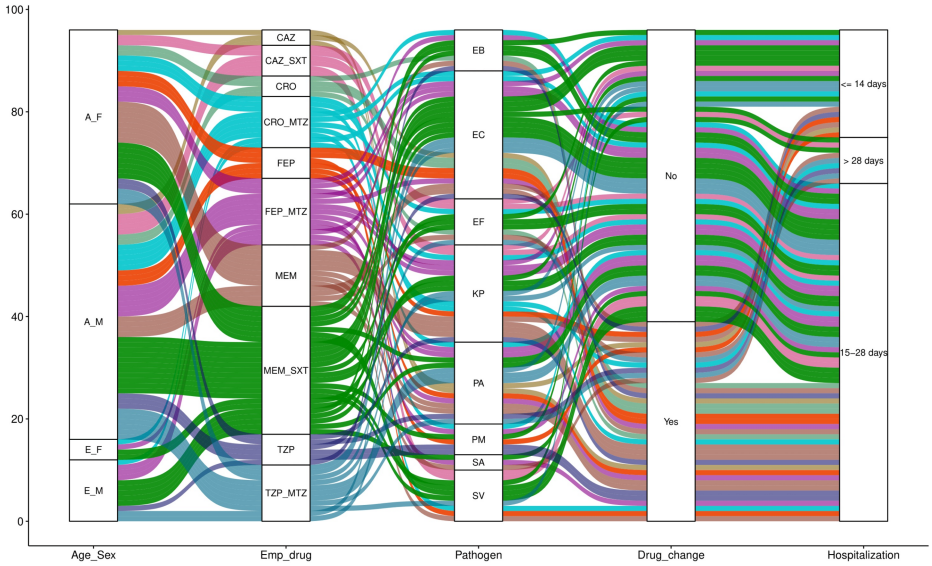


FIGURE 7: Association of empirical antibiotic use among participants with abdominal infections

The alluvial plot illustrates the associations between empirical antibiotic use and gender, age group, detected pathogenic bacteria, changes in drugs per the culture and sensitivity report, and the duration of hospitalization among participants with abdominal infection (n = 96). The y-axis presents the number of participants. The empirical antibiotics (i.e., CAZ, CAZ_SXT, CRO, CRO_MTZ, FEP, FEP_MTZ, MEM, MEM_SXT, TZP, and TZP_MTZ) are presented in different colors. The bandwidths connecting any pair of adjacent parameters are proportional to the number of participants with both parameters.

Age_Sex: age group and gender of the participants, A_F: adult female, A_M: adult male, E_F: elderly female, E_M: elderly male, Emp_drug: empirical antibiotics, CAZ: ceftazidime, CAZ_SXT: ceftazidime + cotrimoxazole, CRO: ceftriaxone, CRO_MTZ: ceftriaxone + metronidazole, FEP: cefepime, FEP_MTZ: cefepime + metronidazole, MEM: meropenem, MEM_SXT: meropenem + cotrimoxazole, TZP: piperacillin-tazobactam, TZP_MTZ: piperacillin-tazobactam + metronidazole, EB: *Enterobacter* spp., EC: *Escherichia coli*, EF: *Enterococcus faecalis*, KP: *Klebsiella pneumoniae*, PA: *Pseudomonas aeruginosa*, PM: *Proteus mirabilis*, SA: *Staphylococcus aureus*, SV: *Streptococcus viridans*, Drug_change: whether the empirical antibiotics have been changed or not (as per the culture and sensitivity report)

The antibiotic codes were derived from the Clinical and Laboratory Standards Institute (CLSI) [25]. This plot was generated using R software version 4.6.1 (R Core Team, Vienna, Austria) [26].

The alluvial plot in Figure *8* demonstrates the associations between empirical antibiotic use and gender, age group, detected pathogenic bacteria, drug changes per the culture and sensitivity report, and the duration of hospitalization among participants with suspected CNS infection. Of the 74 participants with suspected CNS infections, the largest subgroup comprised adult males (23, 31.1%), followed by adult females (22, 29.7%) and elderly males (19, 25.7%). The most commonly prescribed empirical antibiotic therapy was ceftriaxone plus vancomycin (31, 41.9%), followed by ceftriaxone (14, 18.9%), meropenem (7, 9.5%), and piperacillin-tazobactam (7, 9.5%). Of the 74 samples, 39 (52.7%) showed no pathogen growth. The most commonly detected pathogenic bacterium was *Streptococcus pneumoniae* (19, 25.7%), followed by *Neisseria meningitidis* (7, 9.5%). The empirical antibiotic therapy of 41 (55.4%) participants remained unchanged after the culture and AST results were received.

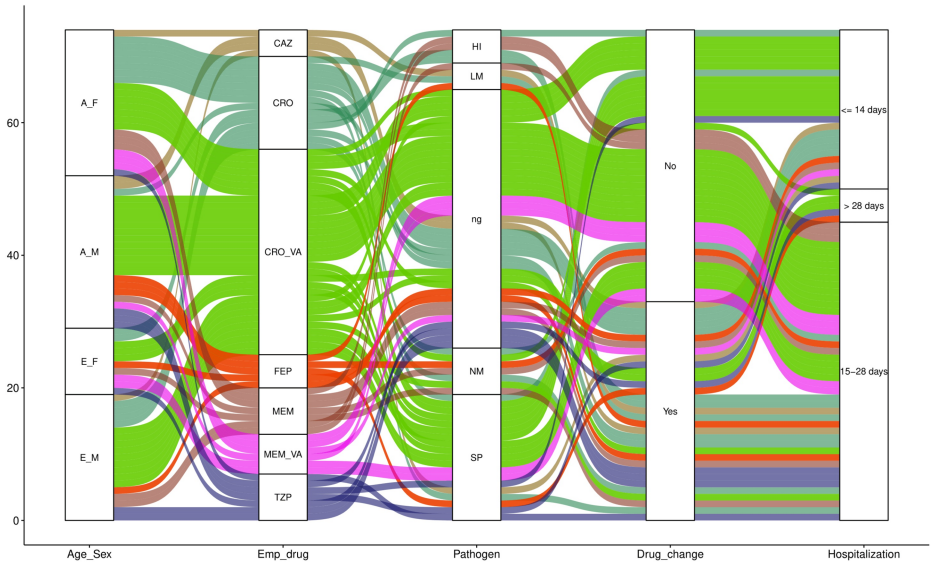


FIGURE 8: Association of empirical antibiotic use among participants with CNS infections

The alluvial plot illustrates the association between empirical antibiotic use and gender, age group, detected pathogenic bacteria, drug changes per the culture and sensitivity report, and the duration of hospitalization among participants with CNS infection (n = 74). The y-axis presents the number of participants. The empirical antibiotics (i.e., CAZ, CRO, CRO_VA, FEP, MEM, MEM_VA, and TZP) are presented in different colors. The bandwidths connecting any pair of adjacent parameters are proportional to the number of participants with both parameters.

CNS: central nervous system, Age_Sex: age group and gender of the participants, A_F: adult female, A_M: adult male, E_F: elderly female, E_M: elderly male, Emp_drug: empirical antibiotics, CAZ: ceftazidime, CRO: ceftriaxone, CRO_VA: ceftriaxone + vancomycin, FEP: cefepime, MEM: meropenem, MEM_VA: meropenem + vancomycin, TZP: piperacillin-tazobactam, HI: *Hemophilus influenzae*, LM: *Listeria monocytogenes*, NM: *Neisseria meningitidis*, SP: *Streptococcus pneumoniae*, ng: no growth, Drug_change: whether the empirical antibiotics have been changed or not (as per the culture and sensitivity report).

The antibiotic codes were derived from the Clinical and Laboratory Standards Institute (CLSI) [25]. This plot was generated using R software version 4.6.1 (R Core Team, Vienna, Austria) [26].

The alluvial plot in Figure *9* demonstrates the associations between empirical antibiotic use and gender, age group, detected pathogenic bacteria, drug changes per the culture and sensitivity report, and the duration of hospitalization among participants with suspected respiratory infections. Of the 276 participants with suspected respiratory infections, 125 (45.3%) were adult males and 100 (36.2%) were adult females. The most commonly administered empirical antibiotic therapy was meropenem (29, 10.5%), followed by ceftazidime-avibactam (28, 10.1%), cefoperazone-sulbactam (26, 9.4%), cefepime (25, 9.1%), and ceftazidime-avibactam plus doxycycline (22, 8.0%). The most common pathogenic bacteria detected were *Klebsiella pneumoniae* (92, 33.3%), followed by *Pseudomonas aeruginosa* (59, 21.4%), *Staphylococcus aureus* (44, 15.9%), and *Escherichia coli* (44, 15.9%). The empirical antibiotic therapy of 140 (50.7%) participants remained unchanged after the culture and AST results were received. None of the combination therapies of ceftazidime-avibactam with doxycycline (22, 8.0%), meropenem with colistin (17, 6.2%), and ceftriaxone plus clarithromycin (15, 5.4%) were substituted. All but two empirical monotherapies (106, 38.4%) were modified based on the culture and AST results. These two participants received either cefoperazone-sulbactam or ceftazidime-avibactam.

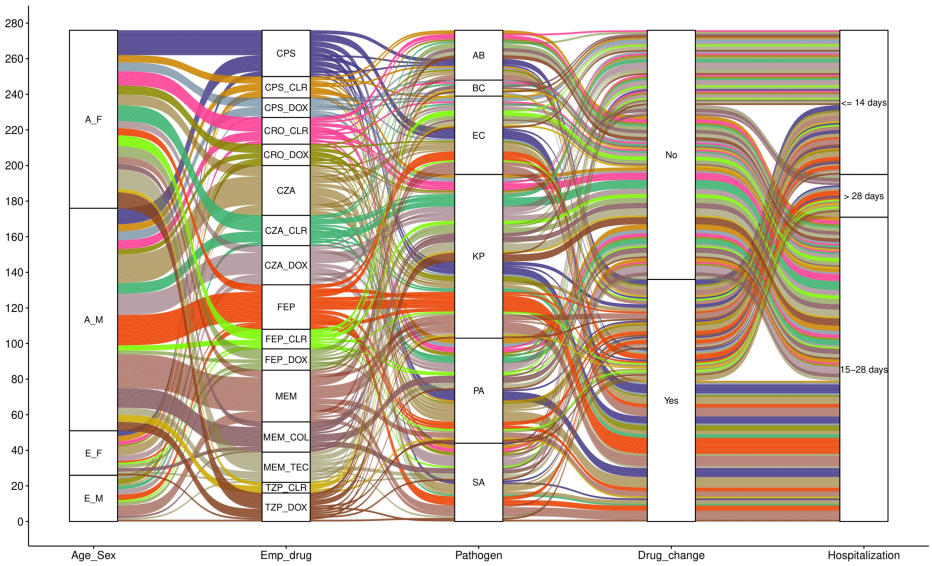


FIGURE 9: Association of empirical antibiotic use among participants with respiratory infections

The alluvial plot illustrates the association between empirical antibiotic use and gender, age group, detected pathogenic bacteria, drug changes per the culture and sensitivity report, and the duration of hospitalization among participants with respiratory infection (n = 276). The y-axis presents the number of participants. The empirical antibiotics (i.e., CPS, CPS_CLR, CPS_DOX, CRO_CLR, CRO_DOX, CZA, CZA_CLR, CZA_DOX, FEP, FEP_CLR, FEP_DOX, MEM, MEM_COL, MEM_TEC, TZP_CLR, and TZP_DOX) are presented in different colors. The bandwidths connecting any pair of adjacent parameters are proportional to the number of participants with both parameters.

Age_Sex: age group and gender of the participants, A_F: adult female, A_M: adult male, E_F: elderly female, E_M: elderly male, Emp_drug: empirical antibiotics, CPS: cefoperazone-sulbactam, CPS_CLR: cefoperazone-sulbactam + clarithromycin, CPS_DOX: cefoperazone-sulbactam + doxycycline, CRO_CLR: ceftriaxone + clarithromycin, CRO_DOX: ceftriaxone + doxycycline, CZA: ceftazidime-avibactam, CZA_CLR: ceftazidime-avibactam + clarithromycin, CZA_DOX: ceftazidime-avibactam + doxycycline, FEP: cefepime, FEP_DOX: cefepime + doxycycline, MEM: meropenem, MEM_COL: meropenem + colistin, MEM_TEC: meropenem + teicoplanin, TZP_CLR: piperacillin-tazobactam + clarithromycin, TZP_DOX: piperacillin-tazobactam + doxycycline, AB: *Acinetobacter baumannii*, BC: *Burkholderia cepacia*, EC: *Escherichia coli*, KP: *Klebsiella pneumoniae*, PA: *Pseudomonas aeruginosa*, SA: *Staphylococcus aureus*, Drug_change: whether the empirical antibiotics have been changed or not (as per the culture and sensitivity report).

The antibiotic codes were derived from the Clinical and Laboratory Standards Institute (CLSI) [25]. This plot was generated using R software version 4.6.1 (R Core Team, Vienna, Austria) [26].

The alluvial plot in Figure *10* demonstrates the associations between empirical antibiotic use and gender, age group, detected pathogenic bacteria, changes in drugs per the culture and sensitivity report, and the duration of hospitalization among participants with suspected skin and soft tissue infection. Of the 46 participants with suspected skin and soft tissue infections, 20 (43.5%) were adult males and 15 (32.6%) were adult females. The most commonly administered empirical antibiotic therapy was piperacillin-tazobactam plus metronidazole (17, 37.0%), followed by piperacillin-tazobactam (10, 21.7%) and meropenem plus tigecycline (8, 17.4%). The most common pathogenic bacteria detected were *Streptococcus pyogenes* (12, 26.1%), followed by *Enterococcus faecalis* (9, 19.6%) and *Pseudomonas aeruginosa* (9, 19.6%). The empirical antibiotic therapy of 24 (52.2%) participants remained unchanged after the culture and AST results were received. None of the regimens combining piperacillin-tazobactam and metronidazole (17, 37.0%) were replaced. All empirical monotherapies (21, 45.7%) were modified based on the culture and AST results.

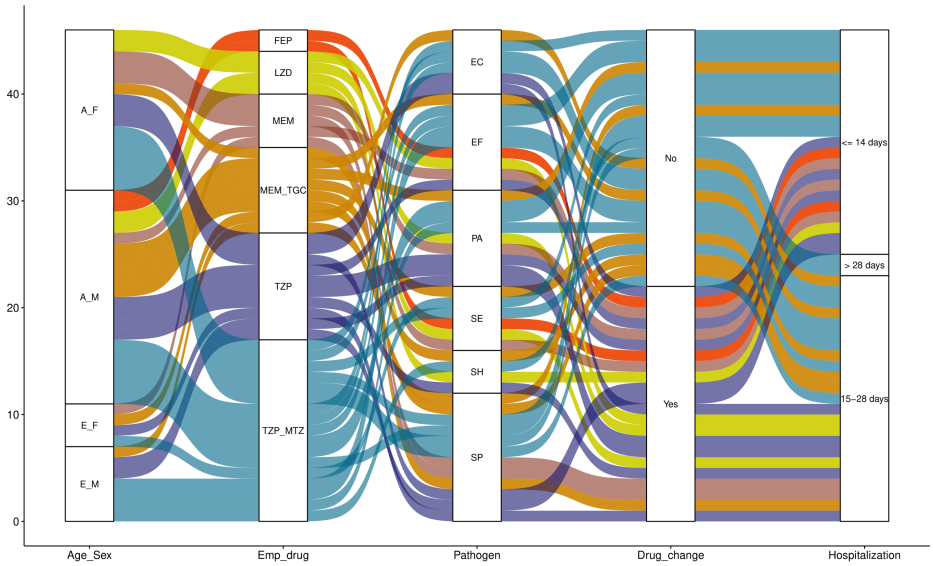


FIGURE 10: Association of empirical antibiotic use among participants with skin and soft tissue infections

The alluvial plot illustrates the association between empirical antibiotic use and gender, age group, detected pathogenic bacteria, drug changes per the culture and sensitivity report, and the duration of hospitalization among participants with skin and soft tissue infection (n = 46). The y-axis presents the number of participants. The empirical antibiotics (i.e., FEP, LZD, MEM, MEM_TGC, TZP, and TZP_MTZ) are presented in different colors. The bandwidths connecting any pair of adjacent parameters are proportional to the number of participants with both parameters.

Age_Sex: age group and gender of the participants, A_F: adult female, A_M: adult male, E_F: elderly female, E_M: elderly male, Emp_drug: empirical antibiotics, FEP: cefepime, LZD: linezolid, MEM: meropenem, MEM_TGC: meropenem + tigecycline, TZP: piperacillin-tazobactam, TZP_MTZ: piperacillin-tazobactam + metronidazole, EC: *Escherichia coli*, EF: *Enterococcus faecalis*, PA: *Pseudomonas aeruginosa*, SE: *Staphylococcus epidermidis*, SH: *Staphylococcus hemolyticus*, SP: *Streptococcus pyogenes*, Drug_change: whether the empirical antibiotics have been changed or not (as per the culture and sensitivity report).

The antibiotic codes were derived from the Clinical and Laboratory Standards Institute (CLSI) [25]. This plot was generated using R software version 4.6.1 (R Core Team, Vienna, Austria) [26].

The alluvial plot in Figure *11* demonstrates the associations between empirical antibiotic use and gender, age group, detected pathogenic bacteria, changes in drugs per the culture and sensitivity report, and the duration of hospitalization among participants with suspected urinary infection. Of the 191 participants with suspected urinary infections, 89 (46.6%) were adult males and 72 (37.7%) were adult females. The most commonly administered empirical antibiotic therapy was ceftriaxone (35, 18.3%), followed by ceftriaxone plus amikacin (29, 15.2%), ceftriaxone plus ciprofloxacin (19, 10.0%), and meropenem plus amikacin (19, 10.0%). The most common pathogenic bacteria detected were *Escherichia coli* (72, 37.7%), followed by *Klebsiella pneumoniae* (43, 22.5%). The empirical antibiotic therapy of 98 (51.3%) participants remained unchanged after the culture and AST results were received. All empirical monotherapies (62, 32.5%) were modified based on the culture and AST results.

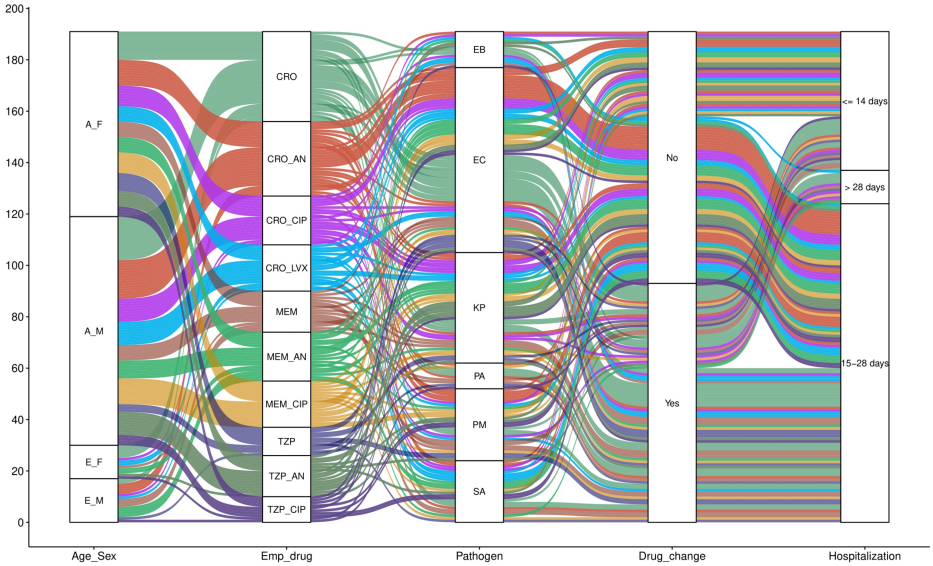


FIGURE 11: Association of empirical antibiotic use among participants with urinary infections

The alluvial plot illustrates the association between empirical antibiotic use and gender, age group, detected pathogenic bacteria, drug changes per the culture and sensitivity report, and the duration of hospitalization among participants with urinary infection (n = 191). The y-axis presents the number of participants. The empirical antibiotics (i.e., CRO, CRO_AN, CRO_CIP, CRO_LVX, MEM, MEM_AN, MEM_CIP, TZP, TZP_AN, and TZP_CIP) are presented in different colors. The bandwidths connecting any pair of adjacent parameters are proportional to the number of participants with both parameters.

Age_Sex: age group and gender of the participants, A_F: adult female, A_M: adult male, E_F: elderly female, E_M: elderly male, Emp_drug: empirical antibiotics, CRO: ceftriaxone, CRO_AN: ceftriaxone + amikacin, CRO_CIP: ceftriaxone + ciprofloxacin, CRO_LVX: ceftriaxone + levofloxacin, MEM: meropenem, MEM_AN: meropenem + amikacin, MEM_CIP: meropenem + ciprofloxacin, TZP: piperacillin-tazobactam, TZP_AN: piperacillin-tazobactam + amikacin, TZP_CIP: piperacillin-tazobactam + ciprofloxacin, EB: *Enterobacter* spp., EC: *Escherichia coli*, KP: *Klebsiella pneumoniae*, PA: *Pseudomonas aeruginosa*, PM: *Proteus mirabilis*, SA: *Staphylococcus aureus*, Drug_change: whether the empirical antibiotics have been changed or not (as per the culture and sensitivity report).

The antibiotic codes were derived from the Clinical and Laboratory Standards Institute (CLSI) [25]. This plot was generated using R software version 4.6.1 (R Core Team, Vienna, Austria) [26].

Discussion

In our study, we assessed the use of empirical antibiotics in patients with sepsis arising from various suspected sources of infection. Most study participants were under 65 years of age. The respiratory and urinary systems were the most common suspected sources of infection. About half of the participants had their empirical antibiotics changed based on the culture reports and AST results. The median WBC count decreased over time. However, its IQR narrowed on day 3 before widening on day 7, remaining narrower than at baseline. Similar trends were observed in SOFA scores. These findings could be attributed to differences in infection sites, host responses, the presence of MDROs, and their antimicrobial susceptibility patterns.

Regardless of the source of infection, beta-lactams were the mainstay of empirical antimicrobial therapy. Ceftriaxone, meropenem, and piperacillin-tazobactam were the most commonly used empirical antibiotics in our study population. Beta-lactam antibiotics exert bactericidal activity by inhibiting bacterial cell wall synthesis [27]. These drugs exhibit time-dependent killing, meaning their bactericidal activity depends on the duration their concentrations remain above the minimum inhibitory concentration (MIC) [27]. Hence, maintaining stable plasma concentrations above the respective MICs for extended periods is essential to ensure optimal dosing [27,28]. Pathophysiological changes in patients with sepsis can affect antibiotic PK-PD [15,29]. For hydrophilic drugs such as beta-lactams, a loading dose is required in patients with sepsis to account for their higher volumes of distribution [29]. Recently, Snow et al. [30] found an association between beta-lactam antibiotics and increased CD4+ lymphocyte viability. These drugs also trigger apoptosis in non-immune cells [30]. These features make beta-lactams first-line empirical antibiotics.

In our study, most empirical antimicrobial combination therapies remained unchanged after culture and AST results were received. This was also true for those with skin and soft tissue infections. We also observed a longer hospital stay among those with antibiotic changes following culture reports and AST results. This

was mainly seen among participants with respiratory and urinary infections. It could be attributed to a reduced host response, the development of bacteremia, septicemia, septic shock, and the need for assisted ventilation and vasopressors. A eubiotic microbiota can protect against colonization by pathogenic bacteria through colonization resistance [31]. Nevertheless, in patients with sepsis, prolonged use of broad-spectrum antibiotics can reduce the commensal intestinal microbiota, leading to the overgrowth of pathogenic bacteria [31,32]. As a tertiary care center, our hospital regularly received referred patients. Hence, the treating clinicians selected broad-spectrum antibiotics to provide coverage against Gram-positive, Gram-negative, and anaerobic organisms. These drugs could have disrupted the eubiotic microbiota and contributed to prolonged hospitalization [32]. These observations were supported by an increase in participants' length of stay despite the drug change and reductions in SOFA scores and WBC counts. Cultures from most participants with suspected CNS infections showed no pathogen growth. In those cases, the decision to continue antibiotic therapy was based on clinical and serological improvements. Participants who showed serological and clinical deterioration despite negative culture results were tested with a cartridge-based nucleic acid amplification test and managed accordingly.

ESKAPE pathogens were prevalent in the participants' microbiological culture reports. These bacteria constitute a substantial proportion of MDROs [19]. These ESKAPE pathogens have developed resistance to beta-lactams, beta-lactam/beta-lactamase inhibitor combinations, tetracyclines, lipopeptides, glycopeptides, fluoroquinolones, macrolides, oxazolidinones, and polymyxins [33]. Antimicrobial stewardship programs (AMSPs) are therefore necessary for the rational use of antimicrobials. AMSPs can delay the development of antimicrobial resistance (AMR) by optimizing antimicrobial use [33].

Strengths and limitations

A major strength of our study was the use of alluvial plots illustrating the associations between empirical antibiotic use and other parameters. Our study had several limitations. First, this study was conducted in a single department at a tertiary care center. This limited the generalizability of the findings. Second, comprehensive assessments of patient outcomes and organ dysfunction throughout the entire hospital stay were beyond the scope of this study, as our primary focus was empirical antibiotic therapy. Therefore, we could not assess pharmacotherapy and the severity of organ impairment over the participants' entire hospital stay. Third, we did not assess the resistance patterns of the detected pathogens because of the heterogeneity of our study population. Fourth, we did not analyze the effects of corticosteroids and vasopressors. Fifth, we could not measure serum lactate and interleukin-6 (IL-6) levels for all participants due to financial constraints.

Conclusions

Beta-lactams were the most commonly used class of antibiotics in our study population. Respiratory and urinary infections were more common among participants than other infection types. The ESKAPE pathogens outnumbered other pathogenic bacteria in this study. Understanding the key determinants of adequate empirical antibiotic therapy is essential for managing patients with sepsis. The suspected site of infection, clinical severity, likely pathogens, local epidemiology, and PK-PD parameters must all be considered when tailoring empirical antibiotic therapy. Inadequate empirical antibiotic therapy leads to poor clinical outcomes, prolonged hospital stays, and increased mortality. Additionally, a multidisciplinary team should be formed to address antibiotic overuse, prevent AMR, and implement an AMSP. We recommend prospective, multicenter studies with larger sample sizes to explore the dynamics of antibiotic use in patients with sepsis across various infection sites.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. Institutional Ethics Committee of Kalinga Institute of Medical Sciences issued approval KIIT/KIMS/IEC/2307/2025. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **AI use statement:** The authors have declared that no AI tools were used during the work or in the drafting of this article. The authors take full responsibility for the work. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Associate Editor authorship:** Jyoti Prakash Sahoo was an Associate Editor for the Cureus Journal of Medical Science at the time of submission. To minimize potential bias, this manuscript was handled independently by an alternate Associate Editor with no conflict of interest, and the author was blinded to and had no access to the peer review process, reviewer identities, or editorial decision-making for this submission. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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