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ICU ANTIBIOTIC THERAPY DYNAMICS: EXAMINING EXTENDED-SPECTRUM ANTIBIOTICS FROM ADMISSION TO DISCHARGE

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Abstract:
This prospective observational study investigates antibiotic prescription patterns among 460 Intensive Care Unit (ICU) patients in Karachi, Pakistan, with a specific focus on extended-spectrum antibiotics. The study analyzes data from the first to the last day of admission, exploring mono and combination antibiotic therapies and their association with extended-spectrum regimens. The findings reveal dynamic shifts in antibiotic utilization, with a notable decrease in combination therapies over the ICU stay. Examining the extended-spectrum antibiotic, the study identifies a significant increase in monotherapy on the last day of admission. This reflects a potential refinement in antibiotic choices as patients progress through their ICU stay. Notably, the association analysis highlights a significant link between extended-spectrum antibiotics and the choice between mono and combination therapy on the last day, emphasizing the evolving nature of antibiotic decision-making in critical care settings. The results underscore the importance of ongoing monitoring and adaptation of antibiotic regimens based on clinical responses and microbial data. The study contributes valuable insights for antibiotic stewardship in the ICU, emphasizing the need for regular reassessment and adjustment of treatment plans. While acknowledging study limitations, including its prospective nature, these findings provide a foundation for future research aimed at optimizing antibiotic use and improving patient outcomes in critical care settings.

Keywords: Extended-spectrum antibiotics, ICU, monotherapy, combination therapy, prospective study

Introduction:

In critical care settings, the judicious use of antibiotics plays a pivotal role in influencing patient outcomes and the management of infections(1). Antibiotics, often referred to as antimicrobial agents, are substances designed to inhibit the growth or destroy microorganisms, particularly bacteria(2). In the complex environment of the Intensive Care Unit (ICU), where patients are susceptible to severe infections, the choice and administration of antibiotics become paramount in ensuring effective treatment while justifying the risk of antibiotic resistance(3).

Extended-spectrum antibiotics, a subset of antimicrobial agents, possess an extended range of activity against a broader spectrum of bacteria, including both Gram-positive and Gram-negative strains(4, 5). These antibiotics are frequently employed in ICU settings to address complex and polymicrobial infections(6). Their utilization requires a delicate balance, as the benefits of extended coverage must be weighed against the potential risks, including the emergence of resistant strains and adverse effects(7).

The ICU serves as a crucible for challenging clinical scenarios, where critically ill patients often present with diverse and severe infections(8). The dynamics of antibiotic prescription in this setting are multifaceted, influenced by factors such as the acuity of the illness, the presence of comorbidities, and evolving microbial susceptibilities(9). The delicate interplay between the need for broad-spectrum coverage and the imperative to avoid overuse highlights the complexity of antibiotic decision-making in the ICU(10, 11).

This study delves into the intricate landscape of antibiotic prescription patterns in the ICU, focusing specifically on extended-spectrum antibiotics(12). As the numbers and types of antibiotics prescribed from the first to the last day of admission were explored, aims were to unravel the evolving patterns in therapy regimens. Understanding the nuances of extended-spectrum antibiotic use in the context of the ICU becomes essential for clinicians striving to optimize patient care while navigating the challenges posed by emerging antibiotic resistance(13).

Methodology:

Study Design: This prospective observational study was conducted to analyze the antibiotic prescription patterns among 460 Intensive Care Unit (ICU) patients in Karachi, Pakistan.

Inclusion Criteria:

1. ICU patients in Karachi, Pakistan.
2. Age 18 years and above.
3. Data from patients with documented antibiotic therapy during their ICU stay.

Exclusion Criteria:

1. Patients below the age of 18.
2. Incomplete or missing data on antibiotic regimens.
3. Patients with unclear documentation of extended-spectrum antibiotic use.

Data Collection:

1. **Patient Demographics:** Collected information includes age, gender, and relevant clinical history.
2. **Antibiotic Regimens:** Data on antibiotic prescriptions on the first and last days of ICU admission were extracted. This includes details on mono-antibiotic therapy and combinations of two, three, or four antibiotics.
3. **Extended-Spectrum Antibiotic Utilization:** Specific focus on extended-spectrum antibiotics, categorizing them into monotherapy and various combinations, was documented for both the initial and final days of ICU admission.
4. **Therapy Changes:** The study examined changes in antibiotic therapy patterns, including complete changes in antibiotic regimens, continuity in prescription, discontinuation and addition scenarios, and the introduction of antibiotics from different classes.

Data Analysis:

1. Descriptive statistics were employed to summarize demographic and clinical characteristics.
2. The frequency and distribution of different antibiotic regimens were analyzed.
3. Changes in extended-spectrum antibiotic therapy were examined to identify patterns and trends.
4. Statistical analysis was conducted using appropriate tools, considering the categorical nature of the data.

Ethical Considerations: This study adhered to ethical guidelines, ensuring patient confidentiality and privacy. Approval from the relevant institutional review board was obtained, and all data were anonymized to maintain the privacy and confidentiality of the patients involved.

RESULTS:

NUMBERS OF ANTIBIOTICS PRESCRIBED ONFIRST AND LAST DAY OF ADMISSION

The antibiotic regimens prescribed in the management of patients in the ICU were categorized into First day and Last day of Admission, further classified by the number of antibiotics prescribed as shown in Table 1 and Figure 1. The distribution of these antibiotic regimens is summarized as follows:

First day antibiotic therapy

- **Mono-Antibiotic Therapy:** The therapy involved the use of a single antibiotic, with 41.7% of patients receiving this regimen.
- **Combination of Two Antibiotics:** A significant portion of patients, 42.7%, received a combination of two antibiotics on first day.
- **Combination of Three Antibiotics:** 14.8% patients received antibiotics a combination of three antibiotics on first day of admission.
- **Combination of Four Antibiotics:** A smaller proportion of patients, 0.8%, were prescribed a combination of four antibiotics on first day of admission.

Last day antibiotic therapy

- **Mono-Antibiotic Therapy:** Among patients receiving antibiotic therapy, 73.1% were treated with a single antibiotic on Last day of admission.
- **Combination of Two Antibiotics:** 23.4% of patients received a combination of two antibiotics on Last day of admission.
- **Combination of Three Antibiotics:** A smaller subset, 3.4% of patients, received antibiotic therapy involving a combination of three antibiotics on Last day of admission.
- **Combination of Four Antibiotics:** No patients were administered a combination of four antibiotics on Last day of admission.

These findings showed the diversity in antibiotic prescribing patterns, with the majority of patients receiving mono-antibiotic therapy more on Last day as compare to first day, while combinations of two antibiotics were also commonly prescribed in both contexts but number of combination of antibiotic were decreased on Last day of admission. On Last day Antibiotic therapy, a significant change can be observed as combinations of antibiotics are often switched to monotherapy as illustrated in Table 1 and Graph 1 The use of combinations involving three or four antibiotics is less frequent, highlighting the importance of modification of antibiotic regimens to individual patient needs and clinical indications

Table 1: Numbers of Antibiotics prescribed on First day and Last day

Antibiotic Regimen	**First dayn (%)**	**Last dayn (%)**
Mono- Antibiotic Therapy	267 (41.7)	468 (73.1)
Combination of two antibiotics	273 (42.7)	150 (23.4)
Combination of three antibiotics	95 (14.8)	22 (3.4)
Combination of four antibiotics	5 (0.8)	-
Total	**640**	**640**

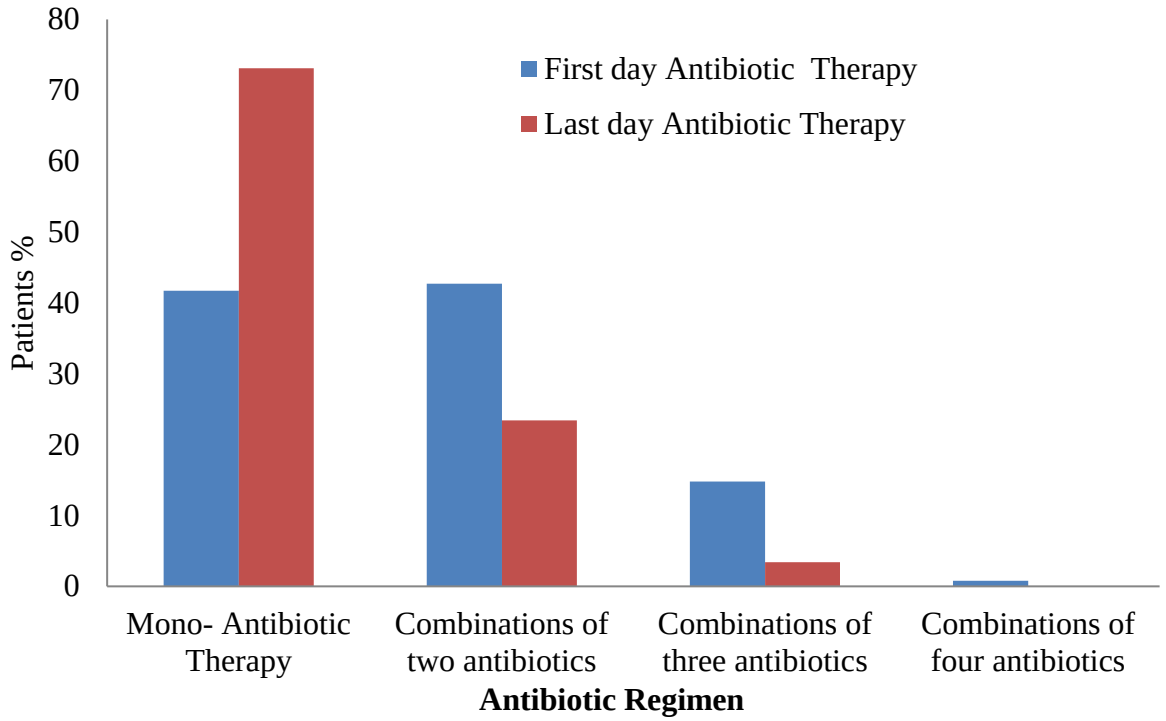

Figure 1: Numbers of Antibiotics prescribed on first day and last day

Distribution of extended-spectrum antibiotic regimen on the First day and Last day of Admission

The antibiotic regimens prescribed for managing ICU patients were categorized into the prescription of extended-spectrum antibiotics on the first day and last day of admission. This classification was further detailed based on the number of antibiotics prescribed, as indicated in Table 2 and Figure 2. Overall, number of extended-spectrum antibiotics was prescribed more in first day than Last day of admission. The distribution of these antibiotic regimens is summarized as follows:

Mono-Antibiotic Therapy: On the first day, among 538 cases, 223 (41.45%) received mono-extended-spectrum antibiotics, while on the last day, among 372 cases, 248 (66.66%) received mono-extended-spectrum antibiotics.

Combination of Two Antibiotics: On the first day, among 538 cases, 219 (40.71%) received combination of two antibiotics in which either one or both are extended-spectrum antibiotics, while on the last day, among 372 cases, 102 (27.41%) received this combination.

Combination of Three Antibiotics: On the first day, among 538 cases, 91 (16.91%) received combination of three antibiotics in which extended-spectrum antibiotics were prescribed, while on the last day, among 372 cases, 22 (5.91%) received this combination.

Combination of Four Antibiotics: On the first day, among 538 cases, only 5 (0.92%) received this combination, while on the last day, none was received this combination.

Table 21: Distribution of the extended-spectrum antibiotic regimen on the first day and last day of admission

Antibiotic Regimen	Extended-spectrum antibiotic at first day n (%)	Extended-spectrum antibiotic at last day n (%)
Monotherapy	223 (41.45)	248 (66.66)
Combination of two antibiotics	219 (40.71)	102 (27.41)
Combination of three antibiotics	91 (16.91)	22 (5.91)
Combination of four antibiotics	5 (0.92)	-
Total	538 (84.1 %)	372 (58.1%)

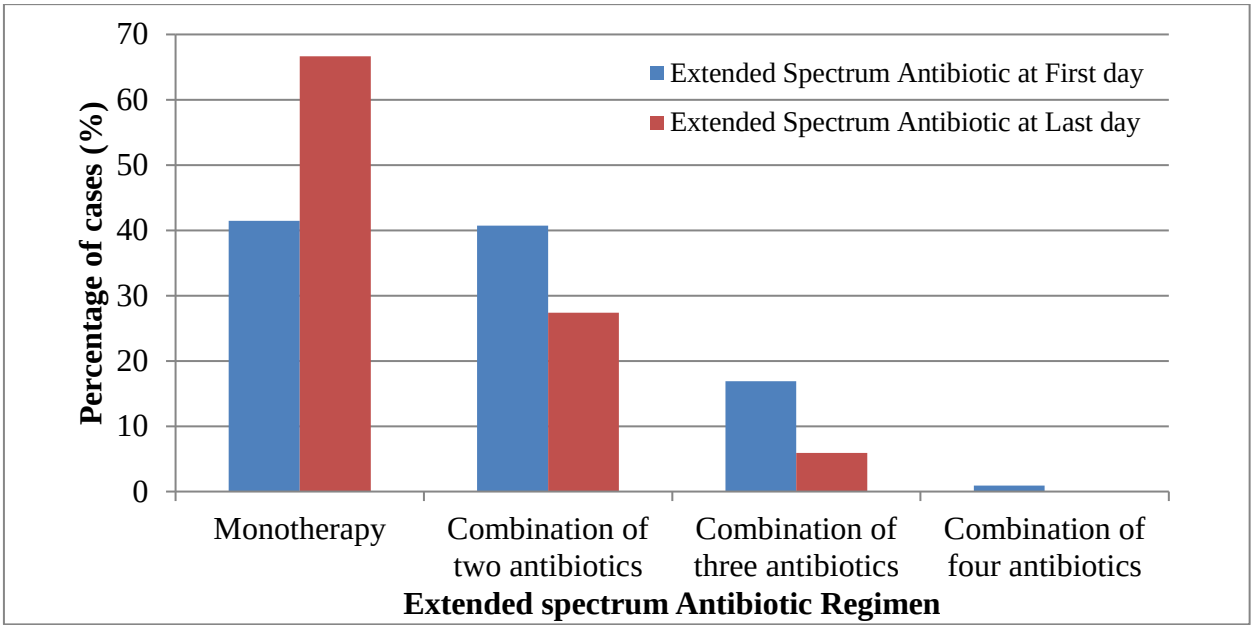

Figure 2: Distribution of the extended-spectrum antibiotic regimen on the first day and last day of admission

The chi-square test results assess the association between the antibiotic regimen (mono or combination) and the prescription of extended-spectrum antibiotics on the first day as depicted in Table 3. These results indicate a statistically non-significant association between the survivors and the use of extended-spectrum antibiotics.

Table3: Association of the extended-spectrum antibiotic regimen on the first day of admission (mono and combination therapy)

Chi-Square Tests on First day	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.100[a]	1	.751		
Continuity Correction[b]	.043	1	.836		
Likelihood Ratio	.100	1	.752		
Fisher's Exact Test				.744	.416
Linear-by-Linear Association	.100	1	.752		
N of Valid Cases	640				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 42.55.
b. Computed only for a 2x2 table

Table 4 shows the chi-square test results assess the association between the antibiotic regimen (mono or combination) and the prescription of extended-spectrum antibiotics on the last day. These

results indicate a statistically significant association between the survivors and the use of extended-spectrum antibiotics on last day.

Table 4: Association of the extended-spectrum antibiotic regimen on the last day of admission (mono and combination therapy)

Chi-Square Tests on Last day	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	18.854[a]	1	.000		
Continuity Correction[b]	18.078	1	.000		
Likelihood Ratio	19.471	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	18.825	1	.000		
N of Valid Cases	640				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 72.03.
b. Computed only for a 2x2 table

CHANGES PATTERNINEXTENDED-SPECTRUM ANTIBIOTIC AND OTHER ANTIBIOTIC THERAPIES

Changes in antibiotic therapy were observed throughout the course of antibiotic treatment in ICU patients. These changes were categorized into following categories, each reflecting a different alteration in the prescribed antibiotic regimen. The distribution of these changes in therapy is summarized as follows and mentioned in Table 5 and Graph 3.

- **Complete Change in Antibiotic Regimen:** A substantial portion of patients, 45.5% of the total 640 cases, and from extended-spectrum 233 (43.31%) underwent a complete change in their regimen underwent a complete change in their antibiotic regimen, indicating a significant shift in their treatment approach.
- **No Change in Antibiotic Therapy:** The majority of patients, constituting 29.5% from over all 640 and 153 (28.44%)from extended-spectrum did not undergo any changes in their antibiotic therapy, maintaining their initial treatment regimen.
- **Discontinuation of Any Antibiotic from Combination:** Among the patients, 13.8% out of 640 and 84 (15.61%) from extended-spectrum experienced discontinuation of at least one antibiotic from their combination therapy.
- **Discontinuation of One Antibiotic and Addition of Another:** 9.7% of patients from 640 and 58 (10.78%) from extended-spectrum had one antibiotic discontinued while another was added to their therapy.
- **Addition of Antibiotic from a Different Class:** A small percentage of patients, 1.6% from 640 cases and 10 (1.85%) from extended-spectrum had an antibiotic from a different class added to their existing regimen.

Table 5: Changes pattern in extended-spectrum antibiotic and other antibiotic therapies

Changes in therapy	No. of Therapy n (%)	Extended-Spectrum Antibiotic n(%)
Complete change in Antibiotic regimen	291 (45.5)	233 (43.31)
No change in Antibiotic regimen	189 (29.5)	153 (28.44)
Discontinuation of any antibiotic from combination	88 (13.8)	84 (15.61)
Discontinuation of one antibiotic and addition of other	62 (9.7)	58 (10.78)
Addition of antibiotic from different class	10 (1.6)	10 (1.85)
Total	**640**	**538**

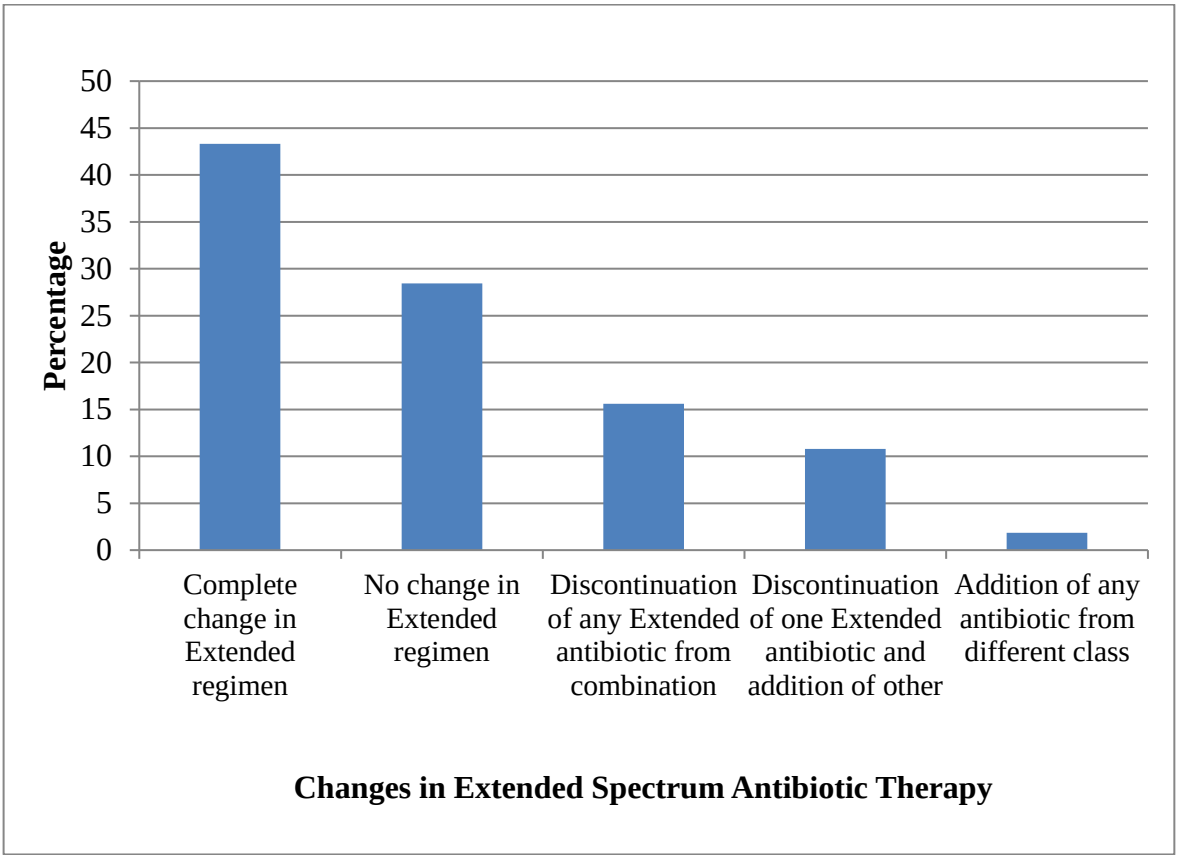

Figure 3: Changes pattern in extended-spectrum Antibiotic Regimen

DISCUSSION:

The findings of this prospective observational study provide valuable insights into the antibiotic prescription patterns among 460 Intensive Care Unit (ICU) patients in Karachi, Pakistan. The analysis focused on the utilization of antibiotics, with a particular emphasis on extended-spectrum antibiotics, shedding light on the dynamics from admission to discharge.

The observed distribution of antibiotic regimens on the first and last days of ICU admission highlights the prevalence of combination therapies, particularly on the initial day. Mono-antibiotic therapy demonstrated a decrease from the first to the last day, while combination therapies, especially those involving two antibiotics, showed a substantial decrease. These patterns may reflect evolving patient conditions and the need for modified antibiotic approaches during the course of ICU stay.

The examination of extended-spectrum antibiotic regimens revealed a notable shift from the first to the last day of admission(14). Monotherapy with extended-spectrum antibiotics increased, indicating a potential refinement in antibiotic choices as patients progressed through their ICU stay(15, 16). However, the decrease in combination therapies involving extended-spectrum antibiotics raises questions about the rationale behind these adjustments and warrants further investigation into the clinical considerations guiding such decisions(17).

The analysis of changes in antibiotic therapy patterns unveiled a considerable proportion of patients experiencing a complete change in antibiotic regimens(18). This suggests a dynamic decision-making process among healthcare professionals, potentially influenced by factors such as evolving clinical conditions, microbial sensitivity results, or adverse effects. Notably, the study identified instances of discontinuation and addition scenarios, emphasizing the need for ongoing assessment and optimization of antibiotic therapy(19).

Understanding the intricate patterns of antibiotic prescription in the ICU setting is crucial for optimizing patient care and addressing challenges such as antibiotic resistance. The observed changes in therapy underscore the importance of regular reevaluation of antibiotic regimens based on clinical responses and microbiological data. Furthermore, the increased utilization of

monotherapy with extended-spectrum antibiotics on the last day of admission may indicate a shift towards more targeted and streamlined antibiotic approaches(19).

The statistical analysis conducted to assess the association of the extended-spectrum antibiotic regimen on the first and last days of admission adds a quantitative dimension to understand the antibiotic prescription patterns(20). On the first day of admission, the Chi-Square tests indicated no significant association between extended-spectrum antibiotic regimens and the choice between mono and combination therapy. This lack of association suggests that, at the initiation of ICU admission, the decision to prescribe extended-spectrum antibiotics may not significantly influence the choice between mono and combination therapy(21).

However, the scenario shifts dramatically on the last day of admission, where the Chi-Square tests demonstrate a highly significant association between the extended-spectrum antibiotic regimen and the choice between mono and combination therapy. The Pearson Chi-Square, Continuity Correction, Likelihood Ratio, and Fisher's Exact Test all yield p-values of 0.000, underscoring the robustness of this association. This implies that as patients progress through their ICU stay, the utilization of extended-spectrum antibiotics becomes closely linked to the decision between mono and combination therapy.

The observed association on the last day of admission raises important clinical considerations. It suggests that healthcare professionals may be more inclined to modify antibiotic regimens, opting for a more targeted approach with extended-spectrum antibiotics as patients approach the end of their ICU stay(21). This shift could be attributed to several factors, including the availability of microbiological data, changes in the clinical presentation of the patient, or a response to evolving resistance patterns.

The significant association identified on the last day of admission emphasizes the role of antibiotic stewardship in ICU settings. As patients near the end of their ICU stay, healthcare providers might intensify efforts to optimize antibiotic therapy, considering the implications for both mono and combination regimens. This finding underscores the dynamic nature of antibiotic decision-making in critical care, reinforcing the need for regular reassessment and adjustment of treatment plans to align with evolving clinical conditions.

Study Limitations and Further Investigations: While these findings contribute valuable insights, it is crucial to acknowledge the limitations of the study, including its prospective nature and reliance on documented data. Future investigations could delve deeper into the factors influencing the association identified, exploring the impact of specific clinical indicators, microbial culture results, and patient outcomes on antibiotic prescription decisions in the ICU.

In summary, the association analysis provides an additional layer of understanding, highlighting the evolving dynamics of antibiotic prescription practices in the ICU. This information can inform future interventions aimed at enhancing antibiotic stewardship and optimizing patient care in critical care settings.

Limitations and Future Directions: It is essential to acknowledge certain limitations, including the prospective nature of the study and the reliance on documented data. The exclusion of patients below the age of 18 limits the generalizability of the findings to adult ICU populations. Future research could explore the factors influencing specific antibiotic choices, including microbial culture results, patient comorbidities, and local resistance patterns.

In conclusion, this study contributes valuable insights into the antibiotic prescription landscape in an ICU setting, emphasizing the need for ongoing monitoring and adaptation of antibiotic regimens. The observed patterns provide a foundation for further research and interventions aimed at optimizing antibiotic use and improving patient outcomes in critical care settings.

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