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Original Research Article

ANTIMICROBIAL DE-ESCALATION IN INTENSIVE CARE UNITS OF A NEWLY ESTABLISHED TERTIARY CARE HOSPITAL - A KEY TOOL IN THE IMPLEMENTATION OF AN ANTIMICROBIAL STEWARDSHIP PROGRAM

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ABSTRACT

Background: Antimicrobial de-escalation (ADE) is a cornerstone of antimicrobial stewardship (AMSP), aimed at limiting the emergence of resistance while preserving clinical outcomes. Data on ADE practices from newly established tertiary care hospitals in India are scarce. This study estimated de-escalation rates of empirical broad-spectrum antibiotics in intensive care units (ICUs) and evaluated their impact on patient outcomes.

Materials and Methods: A prospective observational study was conducted over three months (February–April 2025) in the medical and surgical ICUs of a newly established tertiary care hospital in South India, after Institutional Ethics Committee approval. Consecutively admitted patients who started on empirical antibiotics and had positive microbiological culture results were included and classified into No Change, Escalation, and De-escalation groups; outcomes were compared using Chi-square/Fisher's exact tests.

Results: Of 3235 ICU admissions, only 257 (7.9%) had cultures sent, with a positivity rate of 30% (76 patients). Klebsiella species (32%) and Escherichia coli (22%) were the predominant isolates. Only 41% of samples were sent before starting antibiotics; third-generation cephalosporins were the commonest empirical choice (74%). No patient underwent de-escalation; 76% remained on unchanged therapy, and 24% were escalated. Recovery was numerically higher with escalation (78% vs. 62%) but not statistically significant (p=0.266). Susceptibility status significantly predicted recovery, both within the escalation group (100% vs. 50%, p=0.023) and overall (74% vs. 48%, p=0.038).

Conclusion: No antimicrobial de-escalation occurred in this cohort, highlighting a critical stewardship gap. Organism susceptibility, rather than the decision to escalate or continue therapy, was the stronger determinant of outcome. Strengthening pre-antibiotic culture sampling and instituting structured de-escalation protocols are essential to improve ASP implementation in newly established hospitals.

Keywords: ADE, Antimicrobial de-escalation, AMSP Antimicrobial Stewardship Programme.

INTRODUCTION

Antimicrobial de-escalation (ADE) is defined as the discontinuation of one or more antimicrobial agents in empirical therapy or the replacement of a broad-spectrum antimicrobial agent with a narrow-spectrum antimicrobial agent. There are many controversies in defining antimicrobial de-escalation

(ADE). The European Society of Intensive Care Medicine / European Society of Clinical Microbiology and Infectious Disease societies gave the definition for ADE by which they provide evidence-based guidance to clinicians.[1] Despite the variations in the exact meaning of de-escalation, implementation of ADE in any form has been shown to improve clinical outcomes and reduce the emergence of resistance.[2,3]

Appropriate antimicrobial therapy with control of the infection source is a vital intervention in sepsis management. The 2021 Surviving Sepsis Campaign (SSC) Guidelines suggested a timely and broad-spectrum empirical antimicrobial therapy against all suspected potential pathogens of sepsis.[4] However, exposure to antimicrobials by itself may influence the host microbiota and environmental ecology, thus increasing the selection and emergence of multidrug-resistant (MDR) pathogens due to their broad-spectrum activity, inadequate dose delivery, and prolonged duration of therapy.[5,6] The risk of emergence of new resistance increases for each day of additional exposure to antipseudomonal β-lactam antibiotics, ranging from 2% for meropenem to 8% for cefepime or piperacillin/tazobactam.[7] For these reasons, the 2021 SSC Guidelines recommended daily assessment for antimicrobial de-escalation (ADE) aiming to prevent clinicians from both the overuse of broad-spectrum drugs and the adoption of a fixed therapeutic regimen.[8] Prolonged and inappropriate usage of antibiotics has been explained as the main reason for the emergence of multidrug-resistant pathogens.[9,10,11] Also, the prevalence of infections due to MDR pathogens has been reported to be alarmingly high in low- and middle-income countries when compared to high-income countries. This forms the basis to frame and implement antibiotic stewardship (AMS) programs. AMS strategies include pre-authorization of antibiotics, monitoring of antibiotic usage, involvement of multi-disciplinary teams (physicians, clinical pharmacists, infection control nurses), periodic discussions, etc. De-escalation of antimicrobials has been recommended as an important component of AMS without affecting the clinical outcome of patients.[12,13]

Antibiotic de-escalation (ADE) was initially implemented to reduce the use of broad-spectrum antibiotics in the ICU. It is now the most important component of antimicrobial stewardship and is recommended in international guidelines. Moreover, Guidelines recommend sending appropriate microbiological culture tests before empirical antibiotic therapy. The major advantage of this practice aids in increased chances of identifying the causative organism and, more importantly, deescalating antibiotics to the ones that are effective against the organism. Hence, microbiological sampling is crucial for increasing ADE rates in critically ill patients with infections.[14]

Monitoring the usage of broad-spectrum antibiotics aids in identifying the causes for inappropriate use along with the reasons for non-de-escalation in appropriate circumstances. Hence, this study was carried out to estimate the de-escalation rates of empirical broad-spectrum antibiotics and to identify reasons for non-de-escalation, which will help in the implementation of ASP.

Aim & Objectives: (1) To estimate the De - escalation rates of empirical broad-spectrum antibiotics in the intensive care units. (2) To assess the patient outcome with and without de-escalation. (3) To strengthen the Antimicrobial Stewardship Program.

MATERIALS AND METHODS

This was a prospective observational study conducted for a period of three months after obtaining clearance from the Institutional Ethics Committee. All the patients who are consecutively admitted to Intensive Care Units satisfying the inclusion criteria during the study period will be included.

Inclusion Criteria: Patients admitted to intensive care units who were started on empirical antibiotic treatment with positive microbiological culture reports.

Exclusion Criteria: (1) Patients for whom culture has not been sent. (2) Patients not requiring antibiotic treatment. (3) Patients who did not have positive microbiological culture reports.

The study group was classified into the No change group, Escalation group and Deescalation group. Outcomes like recovery, referral and death rates were compared among the study groups.

Statistical Analysis: Statistical analyses were carried out using the Statistical Package for Social Sciences (SPSS) version 25.0. Continuous variables will be represented as mean and standard deviation. Categorical variables as frequency and percentage. Paired t-test will be used as a statistical test of significance, and p-value <0.05 will be considered statistically significant.

RESULTS

This prospective observational study was conducted over a period of three months from February 2025 to April 2025 in the Medical and Surgical Intensive Care Units of a newly established medical college in South India. There were 3235 admissions to intensive care units during the study period; 2010 (62%) were males, and 1225 (38%) were females. The number of samples received by the microbiology laboratory for culture and sensitivity was 257 (7.9%). The types of samples received were urine (38%, blood (28%, sputum (24% and other samples like body fluids, pus and tracheal aspirate constituted 10%. The culture positivity rate was (76/257) 30%. These 76 culture-positive patients were included in the study group. The most common organism isolated was Klebsiella species 24 (32%),

followed by Escherichia coli 17 (22%), Candida species 13 (17%), Gram-positive organisms 8 (11%), non-fermenters 9 (12%) and other Enterobacterales 5 (7%).

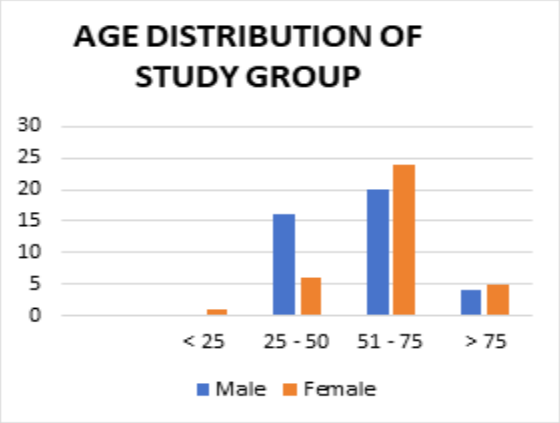

Figure 1: Age Distribution of Study group

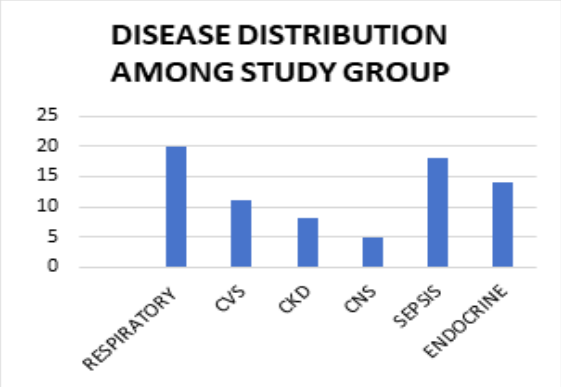

Figure 2: Disease Distribution Among Study group

Figure 1 depicts the age distribution of males and females in the study group. The age group was classified as < 25 years, 25 to 50 years, 51 to 75 years and more than 75 years. Only one female patient was in the age group of <25 years; 16 males and 6 females were in the 25 to 50 years, 20 males and 24 females were in 51 to 75 years, and 4 males and 5 females were in more than 75 years.

Figure 2 presents the disease distribution among the study group. The number of patients with respiratory disease was 20, Cardiovascular disease CVD 11, Chronic Kidney Disease CKD 8, Central Nervous system CNS 5, Sepsis 18 patients and endocrine disorder 14 patients.

Out of 76 patients, in only 31 patients (41%), samples were sent before starting empirical antibiotics. Among the study group, in 56 (74%) patients, third-generation cephalosporins were the most frequently used empiric antibiotic. In the remaining 20 patients (26%), two broad-spectrum, one narrow and one broad-spectrum antibiotics like Piperacillin-tazobactam, Metronidazole and Doxycycline were started.

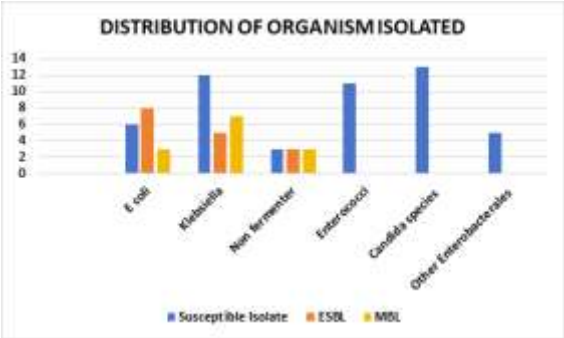

Figure 3: Distribution of Organism Isolated from

Figure 3 demonstrates the distribution of organisms isolated from the samples sent for culture and sensitivity. The organisms isolated were Escherichia coli 17 (22%), Klebsiella pneumoniae 24 (32%), non-fermenters 9, Enterococci 8, Candida species 13 and other Enterobacterales 5. The figure also depicts the resistance patterns like Extended Spectrum Beta Lactamase (ESBL) and Metallo Beta Lactamase (MBL) in the organisms isolated.

Table 1: Duration of ICU stay Among Study group

Duration of ICU Stay	Frequency (n=76)	Percentage
1 – 5 days	34	45%
6 – 10 days	29	38%
>10 days	13	17%

Table 1 shows the duration of stay among the study group. The duration of ICU stay was classified as 1 to 5 days, 6 to 10 days and more than 10 days. About 45% of patients were for 1 to 5 days, 38% were for 6 to 10 days, and 17% were for more than 10 days.

The study group was classified into three groups as follows: No change group, Escalation group and Deescalation group. In the study group, no de-escalation of antibiotics was done.

Table 2: Clinical outcomes by antibiotic strategy group

Study Group	Total	Recovered	Referral/AMA	Expired
No Change (n=58)	S=43, R=15	36 (62%)	6 (10%)	16 (28%)
Escalation (n=18)	S=10, R=8	14 (78%)	0 (0%)	4 (22%)
De-escalation	None	–	–	–

Table 2 presents the classification of the study group into escalation and de-escalation groups with recovery, referral and expiry rates of the study group.

Table 3: Outcomes by susceptibility status within each group

Group	Susceptibility	n	Recovered	Referral/AMA	Expired
No Change	S	43	29 (67%)	2 (5%)	12 (28%)
No Change	R	15	7 (47%)	4 (27%)	4 (27%)
Escalation	S	10	10 (100%)	-	0 (0%)
Escalation	R	8	4 (50%)	-	4 (50%)

Table 3 depicts the outcome status of the patients in the study group based on the treatment done with susceptible or resistant antibiotics.

Table 4: Statistical comparisons

Comparison	Fisher's exact p	Chi-square p
No Change vs Escalation (recovered vs not)	0.266	0.346
No Change vs Escalation (expired vs not)	0.766	0.885
S vs R within No Change Group	0.218	0.263
S vs R within Escalation Group	**0.023***	**0.049***
S vs R overall (both groups combined)	**0.038***	**0.056**

Statistically significant at $p < 0.05$

Table 4 exhibits the statistical comparison between the two groups. The no change and escalation groups were compared for recovery and expiry rate. The outcome of the patients treated with sensitive and resistant antibiotics was also compared.

DISCUSSION

The present study was carried out to study antimicrobial deescalation in Intensive care units of a newly established tertiary care hospital in South India. The study group included 40 (52%) male patients and 36 (48%) female patients, almost equal because of comorbidities like diabetes mellitus, systemic hypertension, and chronic obstructive respiratory diseases. This is similar to the study conducted by Geetha Kaipa, Kiran Babu et al., where the male and female patient ratio was 56% and 44%.[15] In our study, a greater number of patients 58% belonged to the age group of 51 -75 years, which was similar to the study done by Suryasnata Das, Irfanul Haque et al.[19]

The majority of patients in the study group had respiratory illness, followed by sepsis, endocrine abnormality like diabetes mellitus, cardiovascular disease, chronic kidney disease and the least number of patients had CNS diseases; however, in the study conducted by Nitesh Prakash, Nusrat Nabi et al., cardiovascular disease was the major diagnosis, followed by gastrointestinal infections and respiratory infections.[17] The patients were associated with the following comorbidities: diabetes mellitus 28 (37%), systemic hypertension 21 (28%), both Diabetes and hypertension in 12 (16%), COPD in 8 (11%), CAD 4 (5%) and CKD 3 (4%). Sathyamurthy, Rajkumar et al reported that diabetes mellitus is the most common comorbidity, followed by systemic hypertension, CVA, CKD and malignancy.[18] Among the patients, 45% were in ICU for less than 5 days, 38% were in ICU for 6 to 10 days, but only 17% were for more than 10 days; this is very similar to the study done by Nitesh Prakash, Nusrat Nabi et al.[17]

The number of samples received in the Microbiology laboratory for culture and sensitivity was only 7.9% out of intensive care admissions. The culture positivity rate in our study was 30%, but it is 55.5% in Nitesh Prakash, Nusrat Nabi et al. 's study.[17] The culture positivity rate might be increased by increasing the sample size. When compared to ICU admission, samples received by the microbiology laboratory were very few.

The culture positivity was high in pus samples (78%), in Urine 31%, body fluids 33% and respiratory samples 34%, but least in blood samples 5%. But Sathyamurthy, Rajkumar et al identified more isolation in urine samples, followed by blood, pus and other samples.[18] The most common organism isolated was Klebsiella pneumoniae 32%, followed by Escherichia coli 22%; the remaining were non-fermenters, Enterococci and Candida species. Geetha Kaipa and Kiran Babu Redeem reported that Escherichia coli was the most common organism isolated, followed by Klebsiella pneumoniae.[15] The resistance pattern like ESBL and MBL, were more in Escherichia coli 65%, in Klebsiella pneumoniae 50% and in non-fermenters it was 67%.

In 41% of patients, samples were sent to the microbiology laboratory before starting empirical antibiotics. The most commonly used empirical antibiotic was third-generation cephalosporins. But in most of the studies on deescalation, the most common antibiotics used were beta-lactamase inhibitors or carbapenems.[17,19] Based on the patient's clinical status and culture and sensitivity report, the antibiotic was escalated, or it was continued without any change. There was no de-escalation of antibiotics done in the study group. It may be because, in the majority of cases, third-generation cephalosporins were used as empirical antibiotics, followed by escalation if needed. Beta-lactam and beta-lactamase inhibitor combination and carbapenem group of drugs were used wisely for the needed patients.

This study aimed to classify the patients into three groups: No change group, Escalation group and De-

escalation group. Since there was no de-escalation done in the study group, only two groups were compared. 58 patients (76%) were in the No change group, and 18 (24%) were in the Escalation group. In the No change group, the proportion of patients who were treated with sensitive antibiotics was 67%, whereas only 47% of patients recovered who were treated with resistant antibiotics. Similarly, the death rate was equal in the no change group.

In the Escalation group, 100% of patients recovered who were treated with sensitive antibiotics, but 50% of patients were treated with resistant antibiotics.

In this cohort, antibiotic strategy group (no change vs. escalation) was not significantly associated with clinical outcome. Recovery was numerically higher in the Escalation Group (78%, 14/18) compared with the No Change Group (62%, 36/58), and mortality was correspondingly lower (22% vs. 28%), but neither difference reached statistical significance (Fisher's exact $p = 0.266$ for recovery, $p = 0.766$ for mortality). This suggests that, in this sample, the decision to escalate antibiotic therapy did not independently predict a better or worse outcome, though the modest sample size, particularly in the Escalation Group (n=18), limits the power to detect a true effect if one exists.

By contrast, microbiological susceptibility status showed a clearer relationship with outcome. Within the Escalation Group, susceptible (S) isolates were associated with universally favourable outcomes (100% recovery,0%mortality), while resistant (R) isolates were associated with substantially worse outcomes (50% recovery, 50% mortality); this difference was statistically significant (Fisher's exact $p = 0.023$). A similar but non-significant trend was observed within the No Change Group (67% vs. 47% recovery, $p = 0.218$). When susceptibility outcomes were pooled across both groups, patients treated with sensitive antibiotics (S) recovered significantly more often than patients treated with resistant antibiotics (R) (74% vs. 48%, $p = 0.038$ by Fisher's exact test, though this fell just short of significance by chi-square, $p = 0.056$).

Taken together, these findings suggest that organism susceptibility, rather than the clinician's decision to escalate or maintain antibiotic therapy, was the stronger driver of clinical outcome. This is biologically plausible: escalation may only translate into clinical benefit when the causative organism is in fact susceptible to the escalated regimen, whereas escalating therapy against a resistant organism may confer little advantage. The absence of any patients in the De-escalation Group was a major limitation or area for future antimicrobial stewardship intervention.

CONCLUSION

This study highlights a critical gap in antimicrobial stewardship practice at this newly established tertiary care hospital, since not a single patient among the 76 culture-positive ICU admissions underwent antimicrobial de-escalation, with the majority (76%) continued on unchanged empirical therapy and about a quarter (24%) escalated based on clinical status and culture and sensitivity reports. While the choice to continue or to escalate antibiotic therapy was not independently associated with clinical outcome, organism susceptibility emerged as the stronger and statistically significant determinant of recovery of patients treated with susceptible antibiotics fared significantly better than those on resistant regimens, regardless of whether therapy was escalated or left unchanged. These findings, together with the low rate of pre-antibiotic culture sampling (41%) and the overall low culture submission rate (7.9% of ICU admissions), emphasizes the urgent need to strengthen key components of the Antimicrobial Stewardship Program, particularly encouraging early and consistent microbiological sampling before initiating empirical therapy, and instituting structured, protocol-driven daily reassessment for de-escalation opportunities. Multidisciplinary stewardship rounds, prescriber education, and regular audit-and-feedback mechanisms may help translate available culture and sensitivity data into actual de-escalation practice.

Limitations

- This study was conducted at a single, newly established tertiary care centre over a relatively short period of three months, which may limit the generalizability of the findings to other settings with more established antimicrobial stewardship infrastructure.
- The overall sample size, particularly in the Escalation Group (n=18), was small, which may have limited the statistical power to detect true associations between antibiotic strategy and clinical outcome.
- Only7.9% of ICU admissions had samples sent for culture and sensitivity, and just 41%of these were sent before starting empirical antibiotics; this low and inconsistent sampling practice may have introduced selection bias, as culture-negative patients were excluded from analysis.
- Long-term outcomes beyond ICU discharge, such as 28-day mortality, readmission, or recurrence of infection, were not assessed.
- As the study was conducted shortly after the hospital's establishment, antibiotic prescribing patterns and the stewardship program itself were likely still evolving and may not reflect steady-state practice.

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