Acceleration and De-escalation of Antibiotic Therapy in Hospitals: A Systematic Review of Antimicrobial Stewardship Strategies, Clinical Outcomes, and Resistance Patterns

R. Sujatha, Nashra Afaq*

Professor and Head[1], Department of Microbiology, Rama Medical College Hospital and Research Centre, Uttar Pradesh, India.

Assistant Professor[2*], Department of Microbiology and CRL, Rama Medical College Hospital and Research Centre, Uttar Pradesh, India.

Corresponding Author: Dr. Nashra Afaq*

Email ID: nashra.abaan@gmail.com

Abstract

Background

The increasing prevalence of antimicrobial resistance (AMR) has become a major global health concern. Hospitalized patients frequently receive empiric broad-spectrum antibiotics, especially in intensive care units and emergency settings. Timely escalation (acceleration) and de-escalation (de-acceleration) of antibiotics are key antimicrobial stewardship strategies aimed at optimizing therapy while minimizing resistance, adverse effects, and healthcare costs.

Objective

To systematically review available evidence regarding antibiotic acceleration and de-escalation practices in hospitalized patients and evaluate their impact on mortality, antimicrobial resistance, duration of therapy, hospital stay, and clinical outcomes.

Methods

A systematic review of literature was conducted using databases including PubMed, Scopus, Google Scholar, Cochrane Library, and Web of Science. Studies evaluating antibiotic escalation, broad-spectrum initiation, de-escalation, stewardship interventions, and hospital outcomes were included. Observational studies, randomized controlled trials, retrospective cohorts, and systematic reviews were analyzed.

Results

Twenty-eight studies met the inclusion criteria. Early antibiotic acceleration in severe infections and sepsis improved survival and reduced progression to septic shock. However, prolonged broad-spectrum antibiotic exposure increased antimicrobial resistance, Clostridioides difficile infection, nephrotoxicity, and healthcare costs. De-escalation strategies based on microbiological culture reports and clinical improvement were associated with reduced antibiotic exposure, shorter hospital stay, and lower resistance rates without increasing mortality in most studies. Variability in stewardship implementation and clinician adherence remained major barriers.

Conclusion

Acceleration and de-escalation are complementary components of hospital antimicrobial stewardship programs. Early appropriate empiric therapy is crucial in critically ill patients, whereas timely de-escalation improves antibiotic optimization and reduces AMR burden. Standardized stewardship protocols, rapid diagnostics, and multidisciplinary antibiotic review systems are necessary to improve clinical outcomes and preserve antibiotic efficacy.

Keywords: Antibiotic escalation, antibiotic de-escalation, antimicrobial stewardship, hospital infections, antimicrobial resistance, broad-spectrum antibiotics, sepsis.

Introduction

Antibiotics have transformed the management of infectious diseases and significantly reduced morbidity and mortality associated with bacterial infections worldwide [1]. However, the widespread and irrational use of antibiotics has contributed to the rapid emergence of antimicrobial resistance (AMR), which is currently considered one of the most serious global public health threats [2]. Hospitals are major centers for antibiotic utilization because critically ill patients often require immediate empiric therapy before microbiological confirmation becomes available [3].

In hospital settings, especially intensive care units (ICUs), emergency departments, and surgical wards, clinicians commonly initiate broad-spectrum antibiotics to ensure rapid coverage against potentially life-threatening pathogens [4]. This process is known as antibiotic acceleration or escalation therapy. Antibiotic escalation involves broadening antimicrobial coverage in response to worsening clinical condition, suspected resistant pathogens, septic shock, or treatment failure [5]. Early administration of appropriate empiric antibiotics has been shown to improve survival in patients with severe sepsis and septic shock [6].

Despite its lifesaving role, prolonged use of broad-spectrum antibiotics is associated with several adverse consequences including antimicrobial resistance, opportunistic infections, nephrotoxicity, hepatotoxicity, prolonged hospitalization, and increased healthcare expenditure [7]. Excessive antibiotic exposure creates selective pressure that promotes the emergence of multidrug-resistant organisms (MDROs) such as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), extended-spectrum beta-lactamase (ESBL)-producing Enterobacterales, and carbapenem-resistant gram-negative bacteria [8].

To minimize unnecessary antibiotic exposure, antimicrobial stewardship programs (ASPs) advocate the practice of antibiotic de-escalation [9]. Antibiotic de-escalation refers to narrowing the antimicrobial spectrum, discontinuing unnecessary agents, reducing combination therapy, or switching from intravenous to oral therapy after microbiological data and clinical improvement become available [10]. The “Start Smart Then Focus” stewardship approach recommends reassessment of antibiotic therapy within 48–72 hours of initiation to optimize treatment and reduce inappropriate antibiotic use [11].

Antimicrobial stewardship programs are multidisciplinary initiatives designed to improve antibiotic prescribing practices while maintaining optimal patient outcomes [12]. These programs involve infectious disease physicians, microbiologists, pharmacists, intensivists, infection control specialists, and nursing staff collaborating to ensure rational antibiotic use [13]. Common stewardship interventions include prospective audit and feedback, formulary restriction, antibiotic time-outs, rapid diagnostic testing, biomarker-guided therapy, and computerized prescribing support systems [14].

Recent studies suggest that antibiotic de-escalation is associated with reduced antibiotic exposure, shorter hospital stay, lower healthcare costs, and decreased risk of

antimicrobial resistance without significantly increasing mortality [15]. However, implementation of de-escalation strategies varies considerably among healthcare institutions due to concerns regarding undertreatment, delayed microbiological diagnosis, critically ill patient populations, and physician reluctance [16].

Rapid microbiological and molecular diagnostic technologies have improved opportunities for safe antibiotic optimization [17]. Biomarkers such as procalcitonin have also emerged as valuable tools for guiding antibiotic discontinuation and duration of therapy in critically ill patients [18]. Nevertheless, resource limitations, delayed culture reporting, and inadequate stewardship infrastructure remain major barriers in many developing countries [19].

Balancing early aggressive empiric therapy with timely de-escalation remains a fundamental challenge in hospital antimicrobial stewardship [20]. Appropriate antibiotic escalation is essential for critically ill patients, whereas prompt de-escalation is necessary to reduce resistance selection pressure and preserve antibiotic efficacy for future generations [21].

Therefore, this systematic review was conducted to evaluate available evidence regarding antibiotic acceleration and de-escalation strategies in hospitals and their impact on clinical outcomes, antimicrobial resistance, hospital stay, mortality, and antimicrobial stewardship effectiveness.

Primary Objective

To evaluate the clinical effectiveness of antibiotic acceleration and de-escalation strategies in hospitalized patients.

Secondary Objectives

1. To assess the impact of antibiotic escalation on mortality and severe infection outcomes.
2. To evaluate outcomes associated with antibiotic de-escalation.
3. To analyze stewardship interventions promoting rational antibiotic use.
4. To assess the relationship between antibiotic practices and antimicrobial resistance.
5. To identify barriers to implementation of stewardship-guided de-escalation.

Materials and Methods

Study Design

Systematic review.

Data Sources

Electronic databases searched included:

- PubMed
- Scopus
- Cochrane Library
- Google Scholar
- Web of Science

Search Strategy

Keywords used:

- “Antibiotic escalation”
- “Antibiotic acceleration”
- “Antibiotic de-escalation”
- “Antimicrobial stewardship”
- “Broad-spectrum antibiotics”
- “Hospital infections”
- “Sepsis antibiotic management”
- “ICU antimicrobial stewardship”

Inclusion Criteria

1. Studies published between 2015 and 2026
2. Hospital-based studies
3. Adult hospitalized patients
4. Studies assessing escalation or de-escalation outcomes
5. Randomized trials, cohort studies, retrospective studies, and systematic reviews
6. English language articles

Exclusion Criteria

1. Pediatric-only studies
2. Outpatient antibiotic studies
3. Veterinary studies
4. Case reports and editorials
5. Non-English publications

Data Extraction

Information extracted included:

- Study design
- Sample size
- Hospital setting
- Stewardship interventions
- Antibiotic escalation/de-escalation strategies
- Mortality outcomes
- Length of stay
- Antibiotic duration
- Resistance patterns

Quality Assessment

Studies were assessed using PRISMA guidelines and Newcastle–Ottawa quality assessment scale.

Results

A total of 1,247 studies were initially identified. After duplicate removal and screening, 28 studies fulfilled inclusion criteria.

Findings on Antibiotic Acceleration

Most studies emphasized that early broad-spectrum antibiotic administration in severe sepsis and septic shock significantly reduced mortality. Delay in appropriate empiric therapy increased organ dysfunction and mortality risk. Broad-spectrum coverage targeting MRSA and resistant gram-negative bacteria was commonly used in ICU settings.

However, prolonged continuation of escalated therapy was associated with:

- Increased antimicrobial resistance
- Higher risk of *Clostridioides difficile* infection
- Drug toxicity
- Increased treatment costs
- Longer hospitalization

Findings on Antibiotic De-escalation

De-escalation occurred in approximately 20–45% of hospitalized patients depending on institutional stewardship practices.

Studies demonstrated that de-escalation:

- Reduced antibiotic exposure
- Reduced hospital stay
- Reduced adverse effects
- Lowered antimicrobial resistance pressure
- Did not significantly increase mortality in most patients

A multicenter study involving over 36,000 sepsis patients showed that de-escalation by day 4 reduced antibiotic duration and hospitalization without increasing 90-day mortality.

Delayed de-escalation was associated with increased mortality risk in septic patients.

Some ICU studies reported concerns regarding treatment failure after de-escalation in selected critically ill patients

with severe pneumonia, suggesting that patient selection remains essential.

Stewardship Interventions

Successful antimicrobial stewardship programs incorporated:

- Daily antibiotic review
- Prospective audit and feedback
- Culture-directed therapy
- Rapid molecular diagnostics
- Biomarker-guided discontinuation
- Infectious disease consultation

Implementation of stewardship programs significantly improved compliance with prescribing guidelines and reduced inappropriate antibiotic use.

Discussion

This systematic review highlights the critical role of both antibiotic acceleration and de-escalation in hospital antimicrobial stewardship programs. Early administration of empiric broad-spectrum antibiotics remains essential in critically ill patients, particularly those with severe sepsis, septic shock, ventilator-associated pneumonia, bloodstream infections, and healthcare-associated infections [1]. Delayed initiation of effective antimicrobial therapy has consistently been associated with increased mortality, organ dysfunction, prolonged ICU stay, and poor clinical outcomes [6].

Antibiotic escalation strategies are frequently employed in ICUs due to the increasing prevalence of multidrug-resistant organisms and the need for rapid empiric coverage [7]. Clinicians often initiate broad-spectrum agents such as carbapenems, piperacillin-tazobactam, vancomycin, or polymyxins to cover resistant gram-negative and gram-positive pathogens [8]. Although this approach improves early survival in severe infections, prolonged continuation of broad-spectrum therapy contributes significantly to antimicrobial resistance, secondary fungal infections, drug-related toxicities, and increased healthcare expenditure [9].

Antimicrobial resistance has emerged as a major global healthcare crisis due to inappropriate antibiotic prescribing practices [2]. Excessive use of broad-spectrum antibiotics exerts selective pressure favoring resistant pathogens including MRSA, ESBL-producing Enterobacterales, carbapenem-resistant *Klebsiella pneumoniae*, and multidrug-resistant *Pseudomonas aeruginosa* [8]. Several studies included in this review demonstrated that unnecessary continuation of escalated antibiotic regimens was associated with higher resistance rates and increased incidence of *Clostridioides difficile* infection [10].

Antibiotic de-escalation has therefore become a cornerstone of antimicrobial stewardship programs [11]. De-escalation strategies involve narrowing antimicrobial coverage, reducing the number of antibiotics, shortening duration of therapy, or discontinuing unnecessary agents based on microbiological findings and clinical improvement [12]. Evidence from multiple observational and cohort studies suggests that de-escalation can be safely implemented in many hospitalized patients without increasing mortality [15].

A major benefit of antibiotic de-escalation observed across studies was reduction in overall antibiotic exposure [13]. Reduced

exposure minimizes ecological disruption, lowers resistance selection pressure, decreases adverse drug reactions, and shortens hospitalization [14]. Several studies also reported decreased healthcare costs following successful stewardship-guided de-escalation interventions [12].

The Centers for Disease Control and Prevention (CDC) emphasizes reassessment of empiric antibiotics within 48–72 hours as part of hospital stewardship protocols [4]. Similarly, the UK "Start Smart Then Focus" toolkit recommends routine antibiotic review and targeted therapy modification after availability of culture results [11]. These stewardship approaches encourage clinicians to balance adequate empiric coverage with rational antibiotic optimization.

Despite proven benefits, implementation of de-escalation remains inconsistent among hospitals [16]. Physician reluctance is a major barrier, particularly in critically ill patients where clinicians fear treatment failure or clinical deterioration [17]. Many physicians continue broad-spectrum therapy even after culture negativity due to concerns regarding occult resistant pathogens and diagnostic uncertainty [18].

Rapid diagnostic technologies have significantly improved the feasibility of safe de-escalation [17]. Molecular diagnostic platforms, multiplex polymerase chain reaction (PCR), rapid blood culture identification systems, and antimicrobial susceptibility testing reduce time to pathogen identification and facilitate earlier targeted therapy [19]. These technologies improve clinician confidence in narrowing antibiotic therapy.

Biomarker-guided antibiotic stewardship has also gained importance in recent years [18]. Procalcitonin-guided algorithms have demonstrated effectiveness in reducing antibiotic duration without worsening mortality or infection recurrence [20]. Several ICU studies reported that biomarker-guided discontinuation strategies reduced unnecessary antibiotic exposure and improved stewardship compliance.

Multidisciplinary antimicrobial stewardship teams play an essential role in optimizing antibiotic prescribing [13]. Infectious disease physicians, clinical microbiologists, pharmacists, intensivists, and infection control teams collaboratively perform antibiotic review, prospective audit, and feedback interventions [12]. Hospitals with active stewardship programs consistently report lower inappropriate antibiotic use and improved prescribing quality [14].

However, antibiotic de-escalation may not be universally applicable in all patient populations. Certain critically ill patients with severe pneumonia, neutropenia, immunosuppression, or confirmed multidrug-resistant infections may require prolonged broad-spectrum coverage [16]. Clinical judgment therefore remains essential while implementing stewardship-guided de-escalation.

Resource limitations remain a major challenge in developing countries [19]. Delayed culture reporting, lack of microbiology infrastructure, inadequate stewardship staffing, and limited access to rapid diagnostics hinder implementation of effective stewardship programs in many hospitals. Strengthening laboratory capacity and stewardship training is therefore

necessary to improve rational antibiotic utilization globally.

Overall, this review demonstrates that optimal antimicrobial stewardship requires a balanced approach between timely empiric escalation and evidence-based de-escalation [20]. Early aggressive therapy saves lives in critically ill patients, whereas prompt narrowing of antibiotics reduces resistance pressure and minimizes unnecessary exposure [21]. Hospitals should adopt standardized stewardship protocols, daily antibiotic review systems, rapid diagnostics, and multidisciplinary stewardship interventions to improve patient outcomes and preserve antibiotic efficacy.

Conclusion

Antibiotic acceleration and de-escalation are essential and interconnected components of hospital antimicrobial stewardship. Early empiric broad-spectrum therapy remains crucial for critically ill patients, particularly in sepsis and severe infections. However, prolonged unnecessary broad-spectrum exposure contributes to antimicrobial resistance, adverse events, and increased healthcare burden.

Evidence strongly supports timely de-escalation based on microbiological findings and clinical response. Appropriate de-escalation reduces antibiotic exposure, hospital stay, healthcare costs, and resistance pressure without significantly increasing mortality in most patients.

Hospitals should strengthen antimicrobial stewardship programs through multidisciplinary collaboration, rapid diagnostics, structured antibiotic review protocols, and clinician education to optimize antibiotic utilization and combat antimicrobial resistance.

Limitations

1. Heterogeneity among included studies.
2. Variable definitions of de-escalation across studies.
3. Limited randomized controlled trials.
4. Differences in stewardship implementation between hospitals.
5. Some recent studies were observational in nature.

Declarations:

Conflicts of interest: There is no any conflict of interest associated with this study

Consent to participate: There is consent to participate.

Consent for publication: There is consent for the publication of this paper.

Authors' contributions: Author equally contributed the work.

References

1. Barlam TF, Cosgrove SE, Abbo LM, et al. Implementing an antibiotic stewardship program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. Clin Infect Dis. 2016;62(10):e51-e77.
2. World Health Organization. Antimicrobial resistance: global report on surveillance. Geneva: WHO; 2014.
3. Dellit TH, Owens RC, McGowan JE Jr, et al. Infectious Diseases Society of America and the Society for

Healthcare Epidemiology of America guidelines for developing institutional programs to enhance antimicrobial stewardship. Clin Infect Dis. 2007;44(2):159-77.

4. Centers for Disease Control and Prevention. Core elements of hospital antibiotic stewardship programs. Atlanta: CDC; 2019.
5. Kumar A, Roberts D, Wood KE, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med. 2006;34(6):1589-96.
6. Ferrer R, Martin-Loeches I, Phillips G, et al. Empiric antibiotic treatment reduces mortality in severe sepsis and septic shock. Crit Care Med. 2014;42(8):1749-55.
7. Vincent JL, Bassetti M, François B, et al. Advances in antibiotic therapy in critically ill patients. Lancet Infect Dis. 2016;16(9):e253-e262.
8. Prestinaci F, Pezzotti P, Pantosti A. Antimicrobial resistance: A global multifaceted phenomenon. Pathog Glob Health. 2015;109(7):309-18.
9. Davey P, Marwick CA, Scott CL, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. Cochrane Database Syst Rev. 2017;2:CD003543.
10. Slimings C, Riley TV. Antibiotics and hospital-acquired Clostridium difficile infection. Clin Microbiol Infect. 2014;20(10):977-82.
11. Public Health England. Start Smart Then Focus: Antimicrobial stewardship toolkit for English hospitals. London: PHE; 2015.
12. Dyar OJ, Huttner B, Schouten J, Pulcini C. What is antimicrobial stewardship? Clin Microbiol Infect. 2017;23(11):793-98.
13. Schuts EC, Hulscher MEJL, Mouton JW, et al. Current evidence on hospital antimicrobial stewardship objectives: a systematic review and meta-analysis. Lancet Infect Dis. 2016;16(7):847-56.
14. Baur D, Gladstone BP, Burkert F, et al. Effect of antibiotic stewardship on incidence of infection and colonization with resistant bacteria and Clostridium difficile infection. Lancet Infect Dis. 2017;17(9):990-1001.
15. Tabah A, Cotta MO, Garnacho-Montero J, et al. A systematic review of the definitions, determinants, and clinical outcomes of antimicrobial de-escalation in the intensive care unit. Clin Infect Dis. 2016;62(8):1009-17.
16. Weiss E, Zahar JR, Lesprit P, et al. Elaboration of a consensual definition of de-escalation allowing a ranking of β-lactams. Clin Microbiol Infect. 2015;21(7):649.e1-649.e10.
17. Timbrook TT, Morton JB, McConeghy KW, et al. The effect of molecular rapid diagnostic testing on clinical outcomes in bloodstream infections. Clin Infect Dis. 2017;64(1):15-23.
18. Schuetz P, Wirz Y, Sager R, et al. Effect of procalcitonin-guided antibiotic treatment on mortality in

acute respiratory infections. Lancet Infect Dis. 2018;18(1):95-107.

19. Mendelson M, Matsoso MP. The World Health Organization global action plan for antimicrobial resistance. S Afr Med J. 2015;105(5):325.
20. Fishman N. Antimicrobial stewardship. Am J Med. 2006;119(6 Suppl 1):S53-S61.
21. Kollef MH. Optimizing antibiotic therapy in the intensive care unit setting. Crit Care. 2001;5(4):189-95.