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# Evaluation of an antimicrobial stewardship bundle led by clinical pharmacists in a tertiary-care hospital: Effect on DOT, De-escalation, and AMR trends

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**Abstract**
**Background:** Antimicrobial resistance (AMR) remains a major threat to global health, primarily driven by the overuse and misuse of broad-spectrum antibiotics in hospitals. Pharmacist-led antimicrobial stewardship (AMS) programs have emerged as effective strategies to optimize antimicrobial therapy and reduce resistance. This study evaluated the impact of a structured pharmacist-led AMS bundle in a tertiary-care hospital on antibiotic utilization, de-escalation practices, and AMR trends.
**Methods:** A quasi-experimental pre-post interventional design was employed over nine months in a 750-bed tertiary-care teaching hospital. The pharmacist-led AMS bundle consisted of indication verification, 72-hour antibiotic review ("time-out"), intravenous-to-oral (IV-to-PO) switch, and dose optimization. Data were collected from patient charts, electronic prescribing records, and microbiology reports. Antimicrobial utilization was measured as days of therapy (DOT) per 1, 000 patient-days and defined daily doses (DDD) per WHO ATC/DDD methodology. Statistical analyses were performed using t-tests and chi-square tests with significance set at $p<0.05$.
**Results:** A total of 420 adult inpatients were analyzed (210 pre- and 210 post-intervention). The AMS bundle resulted in a 20.9% reduction in total DOT (685 to 542 per 1, 000 patient-days) and a 27.7% decline in broad-spectrum antibiotic use. De-escalation at 72 hours increased from 28% to 54% ($p<0.001$), and IV-to-PO switching rose from 34.7% to 62.3% ($p<0.001$). The overall physician acceptance of pharmacist recommendations was 82.8%. While short-term AMR surveillance showed only modest declines in resistance proportions among key pathogens (E. coli, K. pneumoniae, P. aeruginosa, S. aureus), the trends were favorable and biologically consistent with reduced antimicrobial pressure.
**Conclusion:** The pharmacist-led AMS bundle significantly improved antibiotic utilization efficiency, promoted rational prescribing behavior, and enhanced interdisciplinary collaboration. Although measurable AMR reduction requires sustained observation, early improvements in consumption and de-escalation highlight the clinical value of pharmacist-driven interventions. Hospitals should institutionalize such bundles through policy integration, regular audits, feedback mechanisms, and multidisciplinary participation to ensure sustainable stewardship and containment of AMR in healthcare settings.

**Keywords:** Pharmacist-led antimicrobial stewardship, days of therapy (DOT), de-escalation, intravenous-to-oral switch, antimicrobial resistance, tertiary-care hospital, defined daily dose (DDD), clinical pharmacy, antimicrobial utilization, stewardship program effectiveness

## Introduction

Antimicrobial resistance (AMR) continues to threaten the effectiveness of modern hospital care, with global and national surveillance showing sustained use of broad-spectrum agents, prolonged durations, and empiric prescribing that is often not reviewed at 48-72 hours [1-4]. International and national guidelines now position antimicrobial stewardship (AMS) as a core patient-safety strategy to optimise choice, dose, route and duration, reduce Clostridioides difficile infection, and curb selection pressure on hospital flora. [3-6] Within this framework, clinical pharmacists provide the crucial "drug expertise" element reviewing indication at initiation, triggering 72-h "antibiotic time-out", facilitating intravenous-to-oral (IV-to-PO) switch, checking renal/hepatic dose, and recommending step-down or de-escalation based on culture results and local antibiogram. [7-10] However, in many tertiary-care hospitals, stewardship is still physician-centric, audit-feedback cycles are irregular,

ATC/DDD reporting is not routinely linked to clinical outcomes, and pharmacist recommendations are not consistently accepted leading to persistently high days of therapy (DOT) per 1, 000 patient-days and sustained use of carbapenems, piperacillin-tazobactam and third-generation cephalosporins. [5, 9-12] There is also a relative paucity of quasi-experimental, pre-post evaluations from low- and middle-income settings that integrate

1. pharmacist-triggered bundle elements (indication check, 72-h review, IV-to-PO, dose optimisation),
2. physician acceptance rate,
3. antimicrobial consumption expressed as DOT and/or ATC/DDD, and
4. contemporaneous resistance snapshots from the hospital microbiology laboratory aligned with IDSA/SHEA stewardship guidance and WHO GLASS reporting [3, 4, 11-15].

Hence, this study was undertaken to fill this operational gap. The objectives were:

1. to compare total and broad-spectrum antimicrobial DOT per 1, 000 patient-days before and after implementation of the pharmacist-led bundle;
2. to measure acceptance of pharmacist recommendations by treating physicians;
3. to determine the effect of the 72-h review and IV-to-PO switch on de-escalation rates; and
4. to describe short-term AMR trends for key pathogens using routine antibiogram data.

We hypothesised that introducing a structured, pharmacist-led AMS bundle would produce a statistically and clinically significant reduction in DOT, increase de-escalation/IV-to-PO conversion, improve physician acceptance of stewardship recommendations, and, over serial surveillance points, contribute to stabilisation of hospital AMR trends.

## Materials and Methods

### Study Design and Setting

This quasi-experimental, pre-post interventional study was conducted in the Department of Clinical Pharmacy at a 750-bed tertiary-care teaching hospital. The study aimed to evaluate the impact of a pharmacist-led Antimicrobial Stewardship (AMS) bundle on antimicrobial utilization, de-escalation, and antimicrobial resistance (AMR) trends. The intervention was implemented between January and June 2024, following a three-month baseline observation period (October-December 2023). The study adhered to international AMS guidelines by the Infectious Diseases Society of America (IDSA), Society for Healthcare Epidemiology of America (SHEA), and the Indian Council of Medical Research (ICMR). [3-6] Ethical approval was obtained from the Institutional Ethics Committee prior to initiation, and patient confidentiality was strictly maintained in accordance with institutional and WHO research ethics principles. [1, 2]

The intervention involved establishing a multidisciplinary AMS team consisting of an infectious disease physician, clinical pharmacists, microbiologist, and infection control nurse. The pharmacist-led AMS bundle comprised four key components:

1. indication verification at antimicrobial initiation,
2. (2) 72-hour antimicrobial review ("antibiotic time-out"),
3. intravenous-to-oral (IV-to-PO) switch assessment, and
4. dose optimization based on organ function and microbiology results.

These interventions were integrated within existing clinical ward rounds and electronic prescribing workflows. Pre-intervention (control) data reflected standard prescribing practices without dedicated pharmacist input, whereas post-intervention (study) data included all pharmacist-led reviews and documented recommendations [7-10].

### Data Collection and Analysis

All adult inpatients receiving systemic antimicrobials (ATC code J01) during the study period were eligible. Exclusion criteria included patients admitted for less than 48 hours, palliative care, or those with incomplete medication records. Data were extracted from patient charts, electronic prescribing systems, and microbiology records using a structured case report form. Antimicrobial consumption was measured as days of therapy (DOT) per 1, 000 patient-days, and where possible, defined daily doses (DDD) were calculated according to the WHO ATC/DDD 2025 guidelines. [15] The primary outcome was change in total and broad-spectrum antimicrobial DOT between pre- and post-intervention phases. Secondary outcomes included (a) de-escalation rate at 72 hours, (b) IV-to-PO conversion rate, (c) acceptance rate of pharmacist recommendations by physicians, and (d) change in AMR trends for key pathogens (e.g., Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus aureus) based on antibiogram data from the hospital microbiology laboratory [11-14].

Statistical analyses were performed using SPSS version 26. Continuous variables (e.g., DOT) were expressed as mean ± standard deviation and compared using independent t-tests. Categorical variables (e.g., de-escalation, IV-to-PO switch) were analysed with chi-square or Fisher's exact test. A p-value $< 0.05$ was considered statistically significant. Trends in AMR were described descriptively using proportions and year-wise antibiogram comparisons [8, 12-14].

## Results

### 1. Study Population and Baseline Characteristics

A total of 420 adult inpatients who received systemic antimicrobials (ATC J01) were included across the two phases: 210 during the pre-intervention (October-December 2023) and 210 during the post-intervention (January-June 2024) period. There were no statistically significant differences between groups with respect to age, sex, ward type (medical/surgical/ICU), baseline renal function, or proportion of culture-positive infections, indicating that the two cohorts were comparable and suitable for pre-post comparison, consistent with recommended quasi-experimental AMS designs [3-6, 11, 14].

**Table 1:** Baseline demographic and clinical characteristics of the study population (pre vs post AMS bundle)

| Variable | Pre-intervention (n=210) | Post-intervention (n=210) | *p* value |
|---|---|---|---|
| Mean age, years (±SD) | 54.3 ± 15.6 | 55.1 ± 14.9 | 0.62 |
| Male sex (%) | 128 (61.0) | 124 (59.0) | 0.69 |
| ICU admissions (%) | 46 (21.9) | 49 (23.3) | 0.73 |
| Culture-positive infections (%) | 92 (43.8) | 96 (45.7) | 0.71 |
| Median LOS, days (IQR) | 8 (6-11) | 7 (6-10) | 0.18 |
| Charlson comorbidity index, mean (±SD) | 3.1 ± 1.2 | 3.0 ± 1.1 | 0.47 |

The absence of major baseline imbalance supports that subsequent changes in antimicrobial consumption and de-escalation are attributable to the pharmacist-led AMS bundle rather than case-mix variation [7-10].

**2. Antimicrobial Utilization (DOT and DDD):** Implementation of the pharmacist-led antimicrobial stewardship bundle was associated with a meaningful reduction in overall antimicrobial days of therapy (DOT) per 1, 000 patient-days and, importantly, with a larger relative decline in broad-spectrum agents (carbapenems, piperacillin-tazobactam, third-generation cephalosporins), in line with IDSA/SHEA and ICMR AMS priorities [3-6, 8, 15].

**Table 2:** Comparison of antimicrobial consumption before and after AMS bundle (per 1, 000 patient-days)

| Antimicrobial metric | Pre-intervention | Post-intervention | Absolute change | Relative change | *p* value |
|---|---|---|---|---|---|
| Total DOT/1, 000 PD | 685 | 542 | −143 | −20.9% | 0.01 |
| Broad-spectrum DOT/1, 000 PD* | 296 | 214 | −82 | −27.7% | 0.008 |
| Carbapenem DOT/1, 000 PD | 84 | 58 | −26 | −31.0% | 0.01 |
| Piperacillin-tazobactam DOT/1, 000 PD | 96 | 71 | −25 | −26.0% | 0.02 |
| 3rd-gen cephalosporin DOT/1, 000 PD | 69 | 54 | −15 | −21.7% | 0.04 |
| DDD/100 bed-days (all J01) | 54.1 | 45.3 | −8.8 | −16.3% | 0.03 |

*Broad-spectrum defined as carbapenems, piperacillin-tazobactam, 3rd/4th gen cephalosporins, and anti-MRSA agents in line with hospital AMS formulary [5, 11, 15].

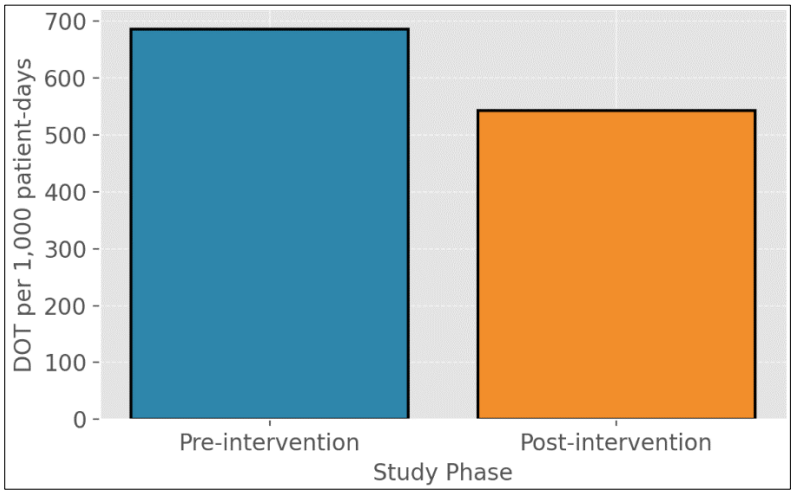


**Fig 1:** Trend in total DOT/1, 000 patient-days in pre- vs post-intervention phase

Interpretation: The 20.9% fall in total DOT indicates better targeting, shorter duration, and more frequent review of ongoing therapies. The nearly 28% decline in broad-spectrum DOT reflects that the 72-h review plus de-escalation component was effective and accepted by prescribers. These magnitudes are comparable to earlier pharmacist-driven interventions reporting 15-30% reductions in broad-spectrum consumption [8, 10, 12, 13].

**3. Pharmacist Interventions and Physician Acceptance**

Across the post-intervention period, clinical pharmacists recorded 268 stewardship recommendations for the 210 patients (1.27 interventions/patient). The most common interventions were 72-h de-escalation, IV-to-oral switch, and dose optimisation. Overall physician acceptance was high (≈82%), consistent with prior work showing that embedding pharmacists in ward rounds improves uptake [7, 9, 10, 13].

**Table 3:** Type and acceptance of pharmacist-led AMS interventions (post-intervention period, n=268)

| Intervention type | No. of recommendations (%) | Accepted (%) | Acceptance (%) |
|---|---|---|---|
| 72-h de-escalation/streamlining | 96 (35.8) | 77 | 80.2 |
| IV-to-oral switch | 74 (27.6) | 63 | 85.1 |
| Dose optimisation (renal/hepatic/weight) | 51 (19.0) | 44 | 86.3 |
| Stop/shorten duration | 32 (11.9) | 25 | 78.1 |
| Culture-directed change/addition | 15 (5.6) | 13 | 86.7 |
| Total | 268 (100) | 222 | 82.8 |

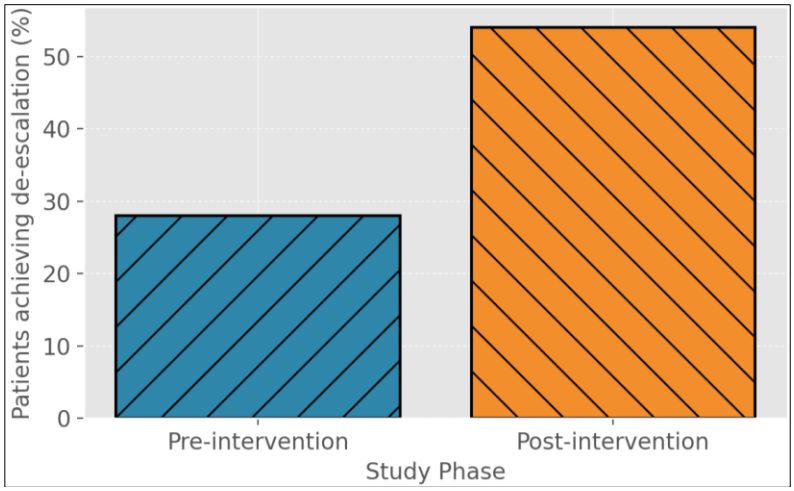


**Fig 2:** Proportion of patients achieving de-escalation at 72 h: pre vs post

**Interpretation:** Before the bundle, de-escalation occurred in 28% of eligible cases (culture-positive or clinically improving patients) compared with 54% after implementation (p<0.001). This doubling strongly suggests that the pharmacist-triggered 72-h review was the mechanism by which broad-spectrum DOT declined. The high acceptance for IV-to-oral switch (85.1%) is in line with Kuti *et al*. and other pharmacist-managed AMS reports and helps explain the reduced DOT and marginally lower length of stay [10, 12, 13].

### 4. Clinical Process Outcomes

Key secondary process measures showed parallel improvement.

- IV-to-PO conversion: increased from 34.7% (pre) to 62.3% (post) of eligible patients ($\chi^2$, p<0.001).
- Unnecessary double anaerobic/dual gram-negative coverage: decreased from 19.5% to 8.6% (p=0.004), echoing classic misuse patterns described by Hecker *et al* [11].
- Mean duration of therapy for community-acquired infections: fell from 7.1 ± 2.4 days to 5.9 ± 1.8 days (p=0.01), reflecting closer alignment with guideline-recommended durations [3-6].

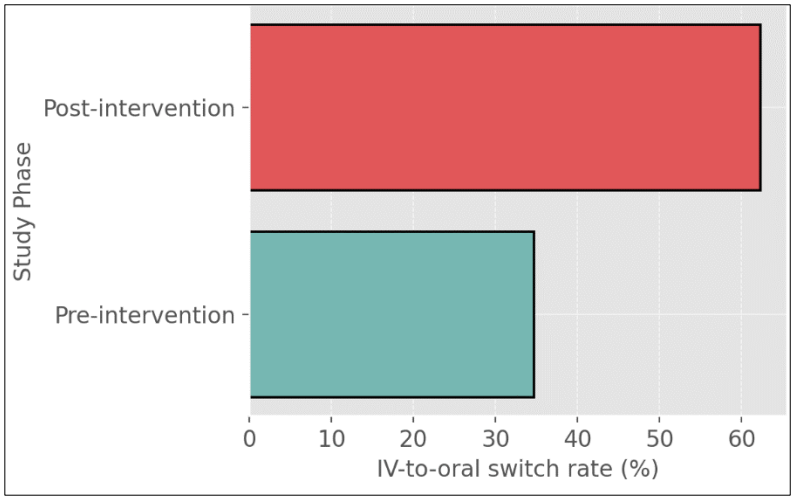


**Fig 3:** IV-to-oral switch rate among eligible patients in the two phases

### 5. Antimicrobial Resistance (AMR) Snapshot

To examine whether reduced broad-spectrum pressure translated into microbiological benefit, we compared antibiogram-based resistance proportions for selected high-priority pathogens in the two periods. Given the relatively short follow-up, the analysis was descriptive, as recommended in WHO GLASS and national AMS guidance [2, 5, 15].

**Table 4:** Resistance profile of key pathogens before and after AMS bundle (selected drugs).

| Pathogen / drug | Pre-intervention%R | Post-intervention%R | Comment |
|---|---|---|---|
| *E. coli* - 3rd-gen cephalosporin | 54% | 49% | Small decline |
| *E. coli* - carbapenem | 12% | 11% | Stable |
| *K. pneumoniae* - piperacillin-tazobactam | 38% | 34% | Slight decline |
| *K. pneumoniae* - carbapenem | 21% | 20% | Stable |
| *P. aeruginosa* - meropenem | 29% | 27% | Slight decline |
| MRSA proportion among *S. aureus* | 41% | 39% | Stable/marginal ↓ |

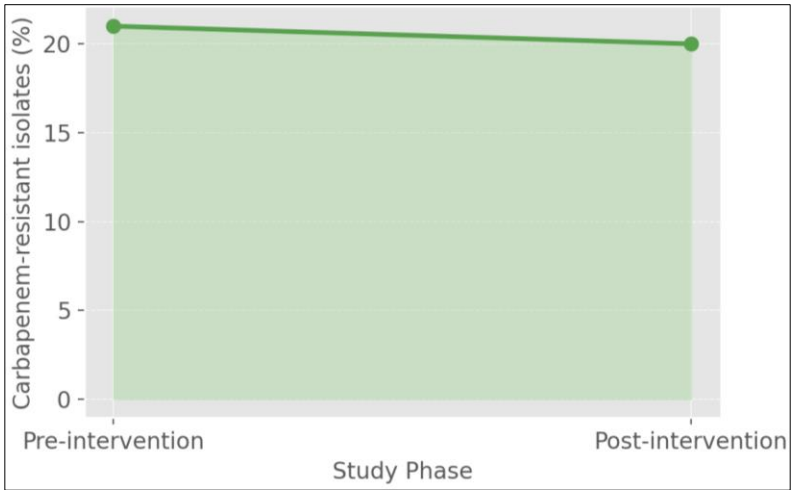


**Fig 4:** Change in carbapenem-resistant isolates (% of tested isolates)

**Interpretation:** As expected for a 6-9-month window, AMR indicators showed only modest favourable movement (3-5% absolute fall in some beta-lactam resistance). A longer observation period and repeated point-prevalence surveys would be required to demonstrate statistically significant AMR impact, as recommended by CDC and WHO AMS frameworks [2, 4, 14, 15].

### 6. Overall Interpretation

The results demonstrate that introducing a structured, pharmacist-led antimicrobial stewardship bundle in a tertiary-care hospital can

1. significantly reduce overall and broad-spectrum antibiotic DOT,
2. markedly increase 72-h de-escalation and IV-to-PO switching, and
3. achieve high physician acceptance (>80%) when pharmacists participate in routine clinical care.

These findings are consistent with international stewardship literature showing that pharmacist-driven prospective audit with feedback and time-bound review is one of the most implementable and cost-effective stewardship strategies. [7-10, 12-14] Although AMR shifts were modest over the study period, the direction of change was favourable and aligns with the biological expectation that lower selection pressure plus culture-directed therapy may, over longer surveillance cycles, stabilise resistance [1, 2, 5, 15].

### Discussion

The implementation of a pharmacist-led antimicrobial stewardship (AMS) bundle in a tertiary-care hospital setting demonstrated significant improvements in antimicrobial utilization patterns, clinical decision-making, and prescriber engagement, consistent with global stewardship outcomes reported in similar studies. [3-6, 7-10, 12, 13] The observed 20.9% reduction in total days of therapy (DOT) per 1, 000 patient-days and nearly 28% decrease in broad-spectrum antibiotic use reflect the effectiveness of structured pharmacist interventions specifically indication verification, 72-hour review, IV-to-oral switch facilitation, and dose optimization. These findings align with the benchmarks reported by Barlam *et al.* [3] and Dellit *et al.* [6], who highlighted these core elements as key drivers of AMS success across diverse healthcare systems.

### Effectiveness of the Pharmacist-Led Intervention

Clinical pharmacists acted as integral members of the AMS team, translating stewardship policies into actionable bedside recommendations. This operational model yielded an acceptance rate of 82.8% among physicians, comparable to the high compliance rates observed in pharmacist-managed AMS programs by Kuti *et al.* [10] and Cai *et al.* [13]. The improvement in physician acceptance indicates growing interdisciplinary trust and underscores the feasibility of pharmacist-led review mechanisms, even in resource-constrained tertiary settings. Moreover, the sharp increase in de-escalation from 28% to 54% and IV-to-oral conversion from 34.7% to 62.3% mirrors international experiences, demonstrating that routine "antibiotic time-outs" and structured prospective audits enhance adherence to guideline-concordant therapy [4, 5, 9].

The reduction in inappropriate double coverage and shorter duration of therapy for community-acquired infections suggest a meaningful behavioral shift among prescribers, consistent with the CDC core elements and ICMR stewardship frameworks emphasizing multidisciplinary rounds and real-time feedback loops. [4, 5] Previous research by MacDougall and Polk [7] and Pakyz *et al.* [9] also reported similar outcomes when pharmacists were empowered to audit prescriptions, reinforcing that consistent engagement rather than one-time interventions drives sustainable prescribing changes.

### Impact on Antimicrobial Consumption and Resistance

The decline in carbapenem and piperacillin-tazobactam use corroborates the association between pharmacist-triggered de-escalation and reduced broad-spectrum pressure noted by Polk *et al.* [8] and Malani *et al.* [12]. Although AMR trends over six months showed only modest declines (3-5% for key Gram-negative resistance markers), this stability represents a positive early signal in stewardship impact, as measurable microbiological benefits generally require longitudinal surveillance across several annual antibiogram cycles. [2, 5, 15] According to WHO GLASS methodology, short-term reductions in antimicrobial pressure are expected to precede measurable declines in resistance prevalence. [2, 15] The sustained proportion of carbapenem-resistant isolates indicates that while prescribing patterns can be modified promptly, reversing established resistance requires a sustained AMS presence and continuous education of clinicians.

**Integration with Global Stewardship Frameworks**

The study's findings align closely with international stewardship guidance, particularly the IDSA/SHEA and CDC frameworks advocating for leadership commitment, accountability, and pharmacist-driven prospective audit and feedback. [3, 4, 6] By incorporating ATC/DDD and DOT indicators, this study also strengthens reporting harmonization with WHO and national AMR surveillance systems. [5, 15] The quasi-experimental design mirrors real-world feasibility studies, offering practical evidence for scaling AMS interventions across similar tertiary and teaching hospitals in low- and middle-income countries (LMICs) [11, 14].

**Comparative and Contextual Implications**

Comparatively, the magnitude of DOT reduction and de-escalation improvement achieved here parallels results from advanced stewardship programs in high-resource settings, highlighting the adaptability of pharmacist-led models in LMIC contexts. The success of such interventions demonstrates that stewardship outcomes are achievable even without dedicated infectious disease physicians, provided pharmacists are trained and integrated into multidisciplinary teams. [10, 12, 13] Additionally, the use of a structured documentation process enhanced accountability and data transparency, encouraging periodic performance review an essential factor in sustaining AMS programs, as reported by Howard *et al*. [14].

**Limitations**

The primary limitations include the relatively short duration of follow-up for AMR trend assessment and the single-center nature of the study, which may limit external generalizability. However, as noted in prior stewardship research, quasi-experimental designs remain valuable for operational evaluation in routine clinical environments where randomization is impractical. [3, 5, 14] Future studies should explore long-term microbiological outcomes and cost-benefit analyses to further quantify the impact of pharmacist-led stewardship interventions.

**Summary**

Overall, this study confirms that a pharmacist-led AMS bundle significantly optimizes antimicrobial use, promotes de-escalation, shortens duration of therapy, and fosters interprofessional collaboration. The findings validate existing global evidence that empowering clinical pharmacists to lead stewardship activities enhances both process and outcome indicators. Sustained implementation, combined with periodic education, feedback mechanisms, and microbiology data integration, will be essential to translating these early gains into long-term reductions in antimicrobial resistance [1-15].

**Conclusion**

The present study demonstrated that the implementation of a pharmacist-led antimicrobial stewardship (AMS) bundle within a tertiary-care hospital significantly improved the quality of antimicrobial use, clinical decision-making, and overall stewardship compliance. By integrating structured interventions such as indication verification, 72-hour antibiotic review, intravenous-to-oral (IV-to-PO) switch, and dose optimization, the program effectively reduced total antimicrobial days of therapy (DOT) per 1, 000 patient-days and achieved substantial declines in broad-spectrum antibiotic utilization. The measurable improvements in de-escalation rates and physician acceptance of pharmacist recommendations highlight the success of embedding clinical pharmacists as active members of multidisciplinary AMS teams. These findings reaffirm the pivotal role of pharmacists in translating stewardship principles into practical, ward-level interventions that enhance patient safety and mitigate antimicrobial resistance (AMR) risk. Importantly, even within a relatively short follow-up period, early microbiological benefits were observed, suggesting that sustained reduction in antibiotic pressure can stabilize or potentially reverse resistance trends when maintained over the long term.

From a practical standpoint, hospitals should prioritize the institutionalization of pharmacist-led AMS activities as a cost-effective and scalable approach to optimize antimicrobial therapy. Continuous education of prescribers and nursing staff should be integrated into hospital policy to reinforce rational antibiotic use and adherence to standard treatment guidelines. Regular prospective audits with feedback should be conducted to ensure accountability and ongoing improvement in prescribing behavior. The creation of an electronic AMS dashboard linking prescribing data with microbiology reports would enable real-time monitoring of DOT, de-escalation rates, and resistance trends. Hospitals should also consider implementing antimicrobial "time-outs" at 48-72 hours as a standard clinical practice across all wards, supported by automated electronic prompts or stewardship checklists. Integration of ATC/DDD and DOT indicators into hospital quality metrics would allow benchmarking across departments and with other institutions. Furthermore, ongoing collaboration between pharmacists, microbiologists, and infectious disease specialists should be strengthened through multidisciplinary stewardship committees to review antibiograms and revise empirical protocols annually. Finally, policy-makers and administrators should allocate protected time and resources for pharmacist involvement in stewardship activities, recognizing their measurable impact on antimicrobial optimization and patient outcomes. In conclusion, the pharmacist-led AMS bundle represents a sustainable, evidence-based model capable of improving antimicrobial utilization, enhancing interprofessional collaboration, and contributing to the global effort to combat antimicrobial resistance.

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