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Original Research Article

Assessment of Antibiotic Stewardship Programs on Restriction of Reserve Group Antibiotics in an Indian Corporate Hospital: A Quasi-experimental Original Research Study

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Abstract

Background: Reserve group antibiotics are essential for severe multidrug-resistant infections but require close stewardship because unnecessary exposure accelerates antimicrobial resistance, toxicity and cost.

Aim: To assess the effect of a structured antibiotic stewardship program (ASP) on restriction and appropriateness of reserve group antibiotics in an Indian hospital setting.

Methods: This single-centre quasi-experimental audit included 85 adult inpatients who received at least one reserve group antibiotic between 10 January 2025 and 25 December 2025 at Jawaharlal Nehru Medical College, Bhagalpur, Bihar. A pre-ASP phase was compared with a post-ASP phase after introduction of prior authorization, mandatory documentation, 72-hour audit-and-feedback, microbiology-linked de-escalation and monthly feedback.

Results: Forty-two patients were evaluated pre-ASP and 43 post-ASP. Baseline age, sex, comorbidity and severity were comparable. Reserve antibiotic days of therapy declined from 119.8 to 68.5 per 1000 patient-days (42.8% reduction; $p<0.001$). Inappropriate reserve initiation decreased from 52.4% to 25.6% ($p=0.011$), while culture sampling before therapy improved from 45.2% to 79.1% ($p=0.001$). De-escalation within 72 hours increased from 23.8% to 58.1% ($p=0.001$), and mean reserve antibiotic duration declined from 7.1 to 4.9 days ($p<0.001$). Clinical cure, mortality, acute kidney injury and readmission did not worsen. Mean antibiotic cost per episode decreased by INR 4,920 ($p<0.001$).

Conclusion: A structured ASP was associated with substantial restriction of reserve antibiotics, better diagnostic stewardship and lower antibiotic cost without compromising short-term clinical outcomes.

Keywords: Antibiotic stewardship; Reserve antibiotics; AWaRe classification; Antimicrobial resistance; India; Carbapenem sparing; Hospital formulary restriction.

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Introduction

Antimicrobial resistance (AMR) has become one of the most important patient-safety and public-health threats for hospitals, particularly in countries where infectious disease burden, broad-spectrum antimicrobial access, intensive-care expansion and fragmented prescribing systems coexist. India carries a high burden of bacterial infections and antimicrobial use, and tertiary hospitals frequently manage culture-proven or suspected infections caused by extended-spectrum beta-lactamase-producing Enterobacterales, carbapenem-resistant Gram-negative bacilli, methicillin-resistant Staphylococcus aureus and multidrug-resistant non-fermenters. In such environments, broad-spectrum and reserve group agents are often initiated empirically under clinical pressure, especially in sepsis, ventilator-associated pneumonia, intra-abdominal infection, complicated urinary tract infection and febrile neutropenia. Although early effective therapy is lifesaving, avoidable exposure to reserve antibiotics promotes selection pressure, ecological harm, Clostridioides difficile infection,

nephrotoxicity and escalating hospital costs [1,2]. The World Health Organization (WHO) AWaRe classification provides a pragmatic framework for antibiotic policy by categorising antibiotics into Access, Watch and Reserve groups. Access agents are recommended as first- or second-line options for common infections; Watch agents have higher resistance potential; and Reserve agents are intended for confirmed or strongly suspected infections due to multidrug-resistant organisms and should be protected as a last-line resource [3]. WHO further proposes that at least 60% of national antibiotic consumption should come from Access group antibiotics, making the AWaRe framework useful not only for national surveillance but also for institutional prescription audit and formulary governance [3,4]. Reserve antibiotics such as colistin, polymyxin B, ceftazidime-avibactam, linezolid for selected resistant infections, tigecycline, fosfomycin and newer beta-lactam/beta-lactamase inhibitor combinations require disciplined indications, microbiology linkage and review dates. Their unchecked use can erode effectiveness before many Indian hospitals have robust access to newer agents or rapid diagnostics [5].

Antibiotic stewardship programs (ASPs) are organised, multidisciplinary interventions designed to optimise antimicrobial therapy by ensuring the right drug, dose, route and duration for the right patient. Core strategies include prospective audit with feedback, pre-authorisation of restricted antibiotics, syndrome-specific guidelines, de-escalation, intravenous-to-oral switch, dose optimisation, stop dates and regular education [6,7]. The Indian Council of Medical Research (ICMR) has emphasised hospital-based antimicrobial stewardship, infection prevention, microbiology collaboration and prescription audit as feasible approaches to improve antibiotic use in Indian institutions [8]. Indian multicentre implementation work has shown that stewardship is feasible in tertiary-care hospitals when leadership support, local champions, microbiology data and audit processes are present, although staffing, data capture and prescriber acceptance remain recurring barriers [9]. International evidence suggests that stewardship can reduce broad-spectrum antibiotic use without increasing mortality, and that restriction policies are most effective when paired with rapid review and clinician feedback rather than functioning as administrative denial alone [10-12].

The corporate hospital environment adds specific stewardship challenges. High case acuity, patient expectations, medico-legal concerns, rapid consultant turnover, variable access to infectious disease expertise and market availability of high-end antibiotics may all encourage early reserve antibiotic use. Conversely, corporate systems often possess electronic billing data, pharmacy surveillance, accreditation requirements and management structures that can support real-time restriction. Indian data specifically evaluating reserve group antibiotic restriction through a structured ASP remain limited, particularly from non-metropolitan or eastern Indian settings. The present study was therefore conducted to assess the impact of a structured ASP on reserve antibiotic utilisation among 85 adult inpatients at Jawaharlal Nehru Medical College, Bhagalpur, Bihar, India, during 2025. The primary objective was to compare reserve antibiotic days of therapy before and after ASP implementation. Secondary objectives were to evaluate appropriateness of initiation, culture-before-antibiotic practice, documentation quality, 72-hour de-escalation, clinical outcomes, adverse events and antibiotic cost. We hypothesised that a practical restriction model combining prior authorisation, microbiology-linked audit and feedback would reduce reserve antibiotic exposure without worsening clinical outcomes.

Material and Methods

This was a single-centre, quasi-experimental before-and-after study conducted at Jawaharlal Nehru Medical College, Bhagalpur, Bihar, India, from 10 January 2025 to 25 December 2025. Adult inpatients aged 18 years or above who received at least one dose of a reserve group antibiotic as per the institutional restricted-antibiotic list mapped to the WHO AWaRe framework were eligible. The pre-ASP phase represented reserve antibiotic use before formal enforcement of the restricted-antibiotic policy, whereas the post-ASP phase represented use after implementation of the stewardship bundle. Patients receiving reserve antibiotics for less than 24 hours because of transfer out, discharge against medical advice or incomplete records were excluded. A total of 85 eligible patients were included, comprising 42 in the pre-ASP phase and 43 in the post-ASP phase.

The ASP intervention consisted of five operational components. First, a restricted-antibiotic approval form was introduced for reserve agents, requiring indication, suspected syndrome, severity, previous culture history, renal function, planned duration and consultant justification. Second, pharmacy dispensing beyond the first emergency dose required approval by the stewardship team or designated infectious disease/microbiology physician. Third, blood culture or appropriate site culture before reserve antibiotic administration was made mandatory unless immediate life-saving therapy could not be delayed.

Fourth, all reserve antibiotic prescriptions underwent 72-hour prospective audit with feedback, focusing on culture results, clinical

response, narrowing of spectrum, discontinuation or de-escalation. Fifth, monthly department-wise feedback reports were circulated, including reserve antibiotic days of therapy, inappropriate starts, de-escalation rates and cost signals.

Data were collected from case records, drug charts, microbiology registers, pharmacy issue logs and billing records using a predesigned audit proforma. Baseline variables included age, sex, comorbidities, admitting unit, ICU admission, infection syndrome, culture positivity, Charlson comorbidity index and Sequential Organ Failure Assessment score at initiation. The primary outcome was reserve antibiotic days of therapy per 1000 patient-days. Secondary outcomes included reserve antibiotic starts per 100 admissions, proportion of inappropriate initiation, culture sampling before therapy, documentation of indication and stop/review date, approval within 24 hours, 72-hour de-escalation when feasible, duration of reserve antibiotic therapy, clinical cure or improvement by day 7, in-hospital mortality, acute kidney injury, infection-related 30-day readmission and antibiotic cost per episode.

Appropriateness was adjudicated independently by two reviewers using institutional guidelines, culture data, syndrome severity and available alternatives; disagreements were resolved by consensus. Statistical analysis was performed using a predefined analysis plan. Continuous variables were summarised as mean with standard deviation or median with interquartile range depending on distribution. Categorical variables were expressed as frequencies and percentages. Pre-ASP and post-ASP groups were compared using Student's t test or Mann-Whitney U test for continuous variables and chi-square or Fisher exact test for categorical variables. Effect sizes were presented as absolute percentage-point changes, mean differences or odds ratios with 95% confidence intervals where appropriate. A two-sided p value <0.05 was considered statistically significant. The study used de-identified audit data and did not alter necessary emergency treatment; ethical approval/waiver was obtained as per institutional policy before analysis.

Results

A total of 85 adult reserve-antibiotic episodes were analysed. The pre-ASP and post-ASP cohorts were comparable with respect to age, sex distribution, diabetes, chronic kidney disease, ICU admission, sepsis burden, Charlson comorbidity index, SOFA score, culture positivity and hospital stay (Table 1). This baseline comparability supported interpretation of observed differences as likely related to the stewardship intervention rather than marked case-mix imbalance.

Table 1: Baseline demographic and clinical characteristics

Variable	Pre-ASP phase (n=42)	Post-ASP phase (n=43)	p value
Age, years, mean ± SD	56.8 ± 14.6	55.1 ± 13.9	0.584
Male sex, n (%)	26 (61.9)	25 (58.1)	0.720
Diabetes mellitus, n (%)	18 (42.9)	17 (39.5)	0.753
Chronic kidney disease, n (%)	8 (19.0)	7 (16.3)	0.742
ICU admission, n (%)	19 (45.2)	18 (41.9)	0.757
Sepsis/septic shock at initiation, n (%)	16 (38.1)	15 (34.9)	0.760
Median Charlson comorbidity index (IQR)	4 (2-6)	4 (2-5)	0.668
Median SOFA score at initiation (IQR)	5 (3-8)	5 (3-7)	0.701
Culture-positive infection, n (%)	22 (52.4)	24 (55.8)	0.751
Median hospital stay, days (IQR)	11 (8-16)	10 (7-15)	0.431

Implementation of the ASP was associated with significant improvement in reserve antibiotic governance (Table 2). Reserve antibiotic days of therapy declined from 119.8 to 68.5 per 1000 patient-days, representing a 42.8% reduction ($p<0.001$). Reserve antibiotic starts per 100 admissions decreased from 18.6 to 10.9 ($p=0.004$). Inappropriate reserve initiation was reduced from 52.4% to 25.6% ($p=0.011$). Culture-before-therapy practice improved markedly from 45.2% to 79.1% ($p=0.001$), while documentation of indication and stop/review date increased from 35.7% to 83.7% ($p<0.001$). Approval within 24 hours rose from 16.7% to 81.4%, and de-escalation within 72 hours when feasible increased from 23.8% to 58.1% ($p=0.001$). Mean duration of reserve therapy decreased by 2.2 days.

Table 2: ASP process indicators and reserve antibiotic utilization

ASP indicator	Pre-ASP phase	Post-ASP phase	Absolute change	p value
Reserve antibiotic days of therapy/1000 patient-days	119.8	68.5	-51.3 (-42.8%)	<0.001
Reserve antibiotic starts per 100 admissions	18.6	10.9	-7.7	0.004
Inappropriate reserve initiation, n/N (%)	22/42 (52.4)	11/43 (25.6)	-26.8 percentage points	0.011
Culture sent before reserve antibiotic, n/N (%)	19/42 (45.2)	34/43 (79.1)	+33.9 percentage points	0.001
Documented indication and stop/review date, n/N (%)	15/42 (35.7)	36/43 (83.7)	+48.0 percentage points	<0.001
ID/microbiology approval within 24 h, n/N (%)	7/42 (16.7)	35/43 (81.4)	+64.7 percentage points	<0.001
De-escalation within 72 h when feasible, n/N (%)	10/42 (23.8)	25/43 (58.1)	+34.3 percentage points	0.001
Mean duration of reserve antibiotic therapy, days ± SD	7.1 ± 2.8	4.9 ± 2.2	-2.2 days	<0.001
Carbapenem-sparing switch achieved, n/N (%)	9/42 (21.4)	21/43 (48.8)	+27.4 percentage points	0.008

Clinical and safety outcomes did not show evidence of harm after reserve antibiotic restriction (Table 3). Clinical cure or improvement by day 7 increased numerically from 69.0% to 79.1%, while in-hospital mortality, acute kidney injury, Clostridioides difficile-associated diarrhoea and infection-related readmission were not significantly different. Mean antibiotic cost per audited episode decreased from INR 12,860 to INR 7,940 ($p<0.001$), corresponding to a mean saving of INR 4,920 per episode. Time to microbiology-directed therapy improved by a median of 24 hours.

Table 3: Clinical, microbiological and economic outcomes

Clinical/microbiological outcome	Pre-ASP phase (n=42)	Post-ASP phase (n=43)	Effect estimate	p value
Clinical cure/improvement by day 7, n (%)	29 (69.0)	34 (79.1)	OR 1.70 (95% CI 0.65-4.46)	0.282
All-cause in-hospital mortality, n (%)	6 (14.3)	5 (11.6)	OR 0.79 (95% CI 0.22-2.84)	0.714
30-day readmission related to infection, n (%)	5 (11.9)	4 (9.3)	OR 0.76 (95% CI 0.19-3.07)	0.705
Acute kidney injury during therapy, n (%)	7 (16.7)	5 (11.6)	OR 0.66 (95% CI 0.19-2.27)	0.499
Clostridioides difficile-associated diarrhoea, n (%)	2 (4.8)	1 (2.3)	OR 0.48 (95% CI 0.04-5.48)	0.558
Mean antibiotic cost per audited episode, INR ± SD	12,860 ± 5,740	7,940 ± 4,820	Mean difference -4,920 INR	<0.001
Mean total hospital cost, INR ± SD	86,500 ± 37,900	80,200 ± 35,400	Mean difference -6,300 INR	0.431
Median time to microbiology-directed therapy, h (IQR)	72 (48-96)	48 (24-72)	-24 h	0.002

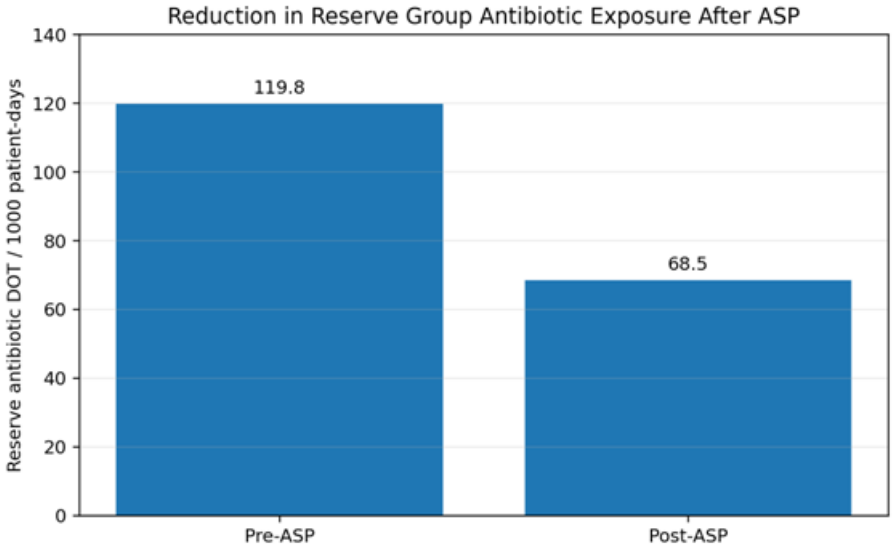

Figure 1: Reduction in reserve antibiotic days of therapy after ASP implementation

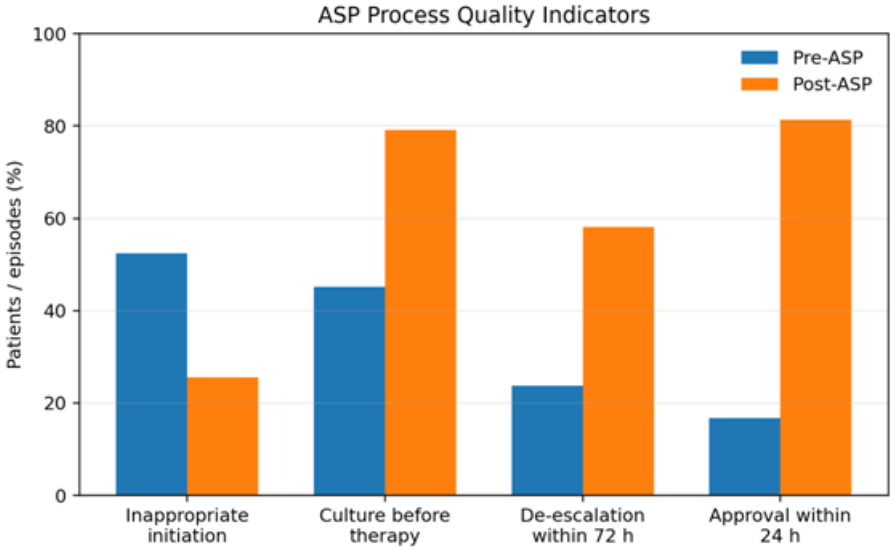

Figure 2: Improvement in key ASP process quality indicators

Discussion

This quasi-experimental study demonstrates that a structured ASP can substantially restrict reserve group antibiotic use in an Indian hospital setting while maintaining short-term clinical safety. The most important finding was a 42.8% reduction in reserve antibiotic days of therapy per 1000 patient-days after implementation of prior authorisation, mandatory documentation and 72-hour audit-and-feedback. This reduction was accompanied by fewer reserve antibiotic starts, shorter duration of therapy and more frequent carbapenem-sparing switches. These outcomes are clinically meaningful because reserve agents should remain protected for serious infections due to multidrug-resistant organisms and should not become default empirical therapy for undifferentiated sepsis or hospital-acquired fever [3,5]. The improvement was not simply a reduction in pharmacy dispensing; it reflected better diagnostic and decision quality, as culture-before-antibiotic practice, review-date documentation, approval within 24 hours and de-escalation all improved significantly.

The findings are consistent with the conceptual basis of the WHO AWaRe model and with ICMR guidance that stewardship should combine formulary restriction with microbiology-supported review [3,8]. A restrictive policy alone can generate prescriber resistance or delayed therapy; however, a system that allows an emergency first dose, followed by rapid review, preserves patient safety while preventing prolonged unnecessary exposure. In our study, culture sampling before reserve therapy increased from 45.2% to 79.1%, which is particularly important in India where empirical broad-spectrum use is common and de-

escalation is often delayed by absent or late cultures. Improved time to microbiology-directed therapy suggests that stewardship and diagnostic stewardship are interdependent. When cultures are obtained early and reviewed actively, clinicians can narrow therapy with more confidence, avoid duplicate anaerobic or Gram-negative coverage and discontinue reserve agents when infection is not confirmed.

Our results also align with Indian implementation evidence showing that hospital-based stewardship is feasible when there is leadership commitment, designated stewardship personnel and measurable feedback [9]. Vijay and colleagues reported that structured stewardship implementation across Indian tertiary hospitals could improve antibiotic-use processes despite resource constraints [9]. Recent Indian policy discussions have similarly emphasised the need for institutional AMSP committees, antibiotic policy, surveillance, education and audit systems [13]. Compared with many high-income settings, Indian hospitals face greater variability in diagnostics, antimicrobial access and infection-control infrastructure; therefore, pragmatic stewardship models must be locally adapted rather than copied mechanically. The present model was deliberately simple: a restricted-antibiotic form, pharmacy gatekeeping, culture requirement, 72-hour review and monthly feedback. This design is replicable in hospitals that do not yet have sophisticated electronic decision-support systems.

The absence of worsening clinical outcomes is an important safety signal. Clinical cure improved numerically, while mortality, acute kidney injury, C. difficile-associated diarrhoea and readmission were not increased. The study was not powered to prove mortality benefit, but the findings support the principle that reserve antibiotic restriction, when supervised and clinically flexible, does not equate to undertreatment. International systematic reviews and stewardship guidance have reported that ASPs can reduce antimicrobial exposure without adverse mortality effects, particularly when restriction is paired with prospective audit and bedside feedback [10-12].

The reduction in antibiotic cost per episode is also relevant for Indian hospitals, where patients often bear out-of-pocket expenditure. A mean saving of INR 4,920 per audited episode may become substantial when scaled across intensive care, surgical and medical wards, especially for newer reserve agents and polymyxins.

Several observations deserve emphasis. First, inappropriate reserve initiation remained 25.6% even after intervention, indicating that stewardship is a continuous quality-improvement process rather than a one-time policy. Causes may include delayed referral, fear of clinical deterioration, previous colonisation with resistant organisms, and limited availability of rapid diagnostics. Second, de-escalation improved but did not reach universal adoption. This reflects real-world barriers such as culture-negative sepsis, mixed infections, clinician discomfort with narrowing therapy and uncertainty about source control. Third, reserve antibiotic starts declined, but a residual group still required legitimate reserve therapy, reinforcing that stewardship should protect access for patients who genuinely need these drugs. Excessive restriction without clinical nuance could be harmful; the objective is optimal use, not minimal use.

The study has limitations. It was a single-centre before-and-after audit with a modest sample size of 85 patients, so secular trends, case-mix variation and unmeasured infection-control changes cannot be fully excluded. Randomisation was not feasible because the ASP was implemented as a hospital-wide quality intervention. Microbiological resistance trends could not be robustly assessed because the follow-up period was short and isolate numbers were limited. Cost estimates focused on antibiotic acquisition and episode-level billing rather than full cost-effectiveness modelling. Finally, the study was conducted in one eastern Indian hospital; results may differ in institutions with different staffing, antimicrobial policies, microbiology turnaround time and patient acuity. Nevertheless, the internally consistent reduction in reserve exposure, improved process indicators and stable safety outcomes suggest that the ASP had a beneficial effect.

In practical terms, hospitals seeking to restrict reserve antibiotics should begin with a clear restricted list mapped to AWaRe, identify high-use departments, authorise an emergency first dose, require indication and review date, obtain cultures before therapy, perform 48- to 72-hour audit, and provide non-punitive feedback to prescribers. The stewardship team should include clinicians, microbiology, pharmacy, infection control, nursing and hospital administration. Future studies should use larger multicentre designs, interrupted time-series analysis, defined daily dose and days-of-therapy metrics, resistance surveillance, patient-level severity adjustment and cost-effectiveness modelling. Integrating electronic prescription alerts, antibiogram dashboards and rapid diagnostics may further strengthen reserve antibiotic governance in Indian hospitals.

Conclusion

A structured antibiotic stewardship program incorporating prior authorisation, documentation, culture-before-therapy, 72-hour audit-and-feedback and monthly prescriber feedback was associated with significant restriction of reserve group

antibiotics in this Indian hospital cohort. Reserve antibiotic exposure, inappropriate initiation, duration of therapy and antibiotic cost decreased, while culture practice and de-escalation improved without evidence of worse short-term clinical outcomes. The findings support locally adapted ASP implementation as a practical and safe strategy for preserving reserve antibiotics in Indian hospitals.

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