Antimicrobial stewardship programme in a trauma centre of a tertiary care hospital in North India: Effects and implementation challenges

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ABSTRACT

Objectives: Hospital-based antimicrobial stewardship programmes (ASPs) aim to optimise antimicrobial use by employing a set of co-ordinated interventions. This study evaluated the implementation challenges of an ASP in a tertiary trauma care centre in India and its effect on antimicrobial prescription.
Methods: A pre- and post-intervention study design was used to compare the effects of the ASP amongst patients admitted during November 2017–January 2018. The appropriateness of antimicrobial prescriptions (dose, route, duration, indication, choice) was evaluated using a validated algorithm. ASP interventions involved daily audit and feedback, restriction on antibacterial usage, daily bedside review, education, and sensitisation activities for residents/nurses. Key implementation challenges and solutions were brainstormed in weekly meetings.
Results: A total of 695 patients were prescribed 1331 antimicrobials. There was a decrease in prophylactic antimicrobial use by 11% ($P < 0.001$). The prescription pattern improved significantly in the intervention phase compared with the pre-intervention phase in terms of duration, choice, indication and route of administration by 8%, 14%, 2% and 8% respectively. Patients in the intervention arm had significantly higher likelihood of receiving antimicrobials for an appropriate duration (aOR = 2.1, 95% CI 1.3–3.6; $P = 0.004$) and reason (aOR = 2.4, 95% CI 1.3–4.3; $P = 0.003$). Challenges identified in implementation included absence of an electronic recording system and inadequate orientation of treating doctors regarding rational antimicrobial use.
Conclusions: The ASP demonstrated significant improvement in antimicrobial usage. This model may be replicated in other hospital settings to promote rational use of antimicrobials.

1. Introduction

In recent years, the use of antimicrobials has grown steadily worldwide, driven mainly by the overwhelming demand due to higher spending capacities of health systems and individuals, higher hospitalisation rates and a higher incidence of hospital-acquired infections [1]. Besides the benefits, irrational use of antimicrobials by mankind has proven to be fatal, leading to the development of antimicrobial resistance, which threatens

the effective prevention and treatment of an ever-increasing range of infections caused by bacteria, parasites, viruses and fungi.

Inappropriate antimicrobial use leads to longer hospital stay, delayed recovery, high mortality and, ultimately, high out-of-pocket expenditure [2,3]. A recent Cochrane review reported that 43% of inpatients were prescribed antimicrobials inappropriately in hospital settings [4]. Optimising the use of antimicrobials is thus included as one of the five objectives in the 'Global action plan on antimicrobial resistance' by the World Health Organization (WHO) [5]. Along the same lines, India has recently launched a national action plan on antimicrobial resistance [6].

In response to this pressing public-health issue, there has been an increased focus on the judicious use of antimicrobial agents. Hospital-based antimicrobial stewardship programmes (ASPs) aim to optimise the use of antimicrobials by employing a set of co-ordinated interventions, including: surveillance of antimicrobial use in health facilities; qualitative evaluation of prophylaxis and treatment in individual patients; monitoring of local antimicrobial susceptibility patterns; promotion of institutional guidelines; and education [7]. ASPs result in a significant decrease in antimicrobial consumption and costs, with the benefit being higher in the critical care setting, along with improvement in the overall hospital length of stay [8]. Different packages of ASP interventions have been tried in different settings with mixed success. A recent Cochrane review stated that stewardship interventions are effective in increasing compliance with antimicrobial policy and reducing the duration of antimicrobial treatment [4]. The review also encouraged that future research should focus on assessing different stewardship interventions. Developing countries have very few examples of functional ASPs in hospital settings. The impact of ASPs in reducing antimicrobial use and decreasing double anaerobic cover in a tertiary care hospital was recently demonstrated [9]. Considering the diverse nature of various departments in a tertiary care centre, we proposed interventions that are tailored to the unit/setting under consideration [10].

Among some of the most dynamic environments of a health facility, the trauma centre has a special place. The top priority is stabilisation of patients in a short interval, and this period is even shorter and more critical if the patient has been referred from a far-off health facility. Antimicrobial therapy is frequently prescribed in severe trauma patients as empirical or prophylactic therapy as a result of many factors such as the patient's clinical status, the severity of injuries, the type of surgical procedure performed, nosocomial infections and as a part of an overcautious treatment protocol. The Advanced Trauma Centre (ATC) in the Postgraduate Institute of Medical Education and Research (PGIMER) (Chandigarh, India), a government tertiary care teaching hospital in North India, is one such unit with a high patient load. Previous studies from PGIMER have reported a large proportion of treatment cost being attributed to antimicrobials [11,12], although little information is available on antimicrobial usage, patterns and justification for use, especially among trauma patients. Therefore, this study was conducted with the aim of studying the effectiveness of ASP interventions on the pattern and appropriateness of antimicrobial usage, especially in a trauma care setting, and documenting the implementation-related challenges therein.

2. Methods

2.1. Study design

A pre- and post-intervention study comparing the effect of an ASP intervention package was performed.

2.2. Study settings

2.2.1. General setting

The study was conducted at PGIMER Chandigarh, a government tertiary care teaching hospital with an inpatient capacity of approximately 2000 beds, situated in the north-western part of India. Being a tertiary care hospital in the region, the hospital caters to a wide variety of patients mainly from the states of Haryana, Punjab, Chandigarh, Himachal Pradesh, Jammu and Kashmir, Western Uttar Pradesh and Uttarakhand. Every year nearly 2.4 million patients visit the hospital. In addition, superspecialty centres serve 85 000 patients annually. The hospital is also involved in teaching and training of undergraduate, postgraduate and PhD students.

2.2.2. Specific setting

The ATC located within the hospital complex has almost 150 beds including specialised intensive care units. The trauma centre has a 100% occupancy rate throughout the year; in the period 2015–2016 approximately 42 000 inpatients and 89 500 outpatients were treated at this centre. The ATC is managed by the Department of Hospital Administration, senior casualty medical officers, specialists and consultants from various specialty departments. The majority of cases are handled by the Department of Orthopaedics. Emergency services are provided round the clock by a team of doctors including junior and senior residents along with faculty from the department. Apart from doctors, functioning of the ATC is largely supported by nursing and paramedical staff.

2.3. Study period

The study was conducted between September 2017 and May 2018.

2.4. Study population

All patients admitted as an inpatient for >24 h in the ATC of PGIMER under the Department of Orthopaedics during November 2017 (pre-intervention phase) and December 2017–January 2018 (intervention period) were included in the study.

2.5. Data collection

The study was planned in two phases, including a pre-intervention phase and an intervention phase. Before initiation of the study, an expert technical committee was created (for the purpose of this study only). The expert committee consisted of senior faculty (from the Departments of Pharmacology, Microbiology, Orthopaedics, Critical Care and Hospital Administration of PGIMER) who are already part of the institute's antimicrobial stewardship committee. Their role was to guide the use of antimicrobials for their appropriateness in the ATC.

2.5.1. Pre-intervention phase

During the pre-intervention phase, baseline data were collected to determine the prevalent antibiotic prescription practices in the ATC. The admission files of patients who were admitted for >24 h under the Department of Orthopaedics in the ATC during November 2017 were reviewed. The principal investigator (MV) collected the data using a structured data collection pro forma. Files of some patients who were transferred out were accessed from the medical records department after seeking due permission.

2.5.1.1. Assessment of appropriateness of antimicrobial use. The appropriateness of antimicrobial prescriptions was evaluated

according to the available departmental antimicrobial policy (Table 1), microbiological findings if available, clinical condition, co-morbidities, history of drug allergy and adverse drug reactions. The appropriateness of each prescription was first assessed by the primary investigator after receiving necessary training and was then re-assessed by the expert technical committee. Appropriateness of the antimicrobial prescription was systematically evaluated with the help of a validated method based on a set of criteria initially reported by Gyssens et al. [13] and modified by Willemsen et al. [14]. The following criteria were used.

(i) Inappropriate indication: prescription of antimicrobials without the presence of an infection, or prescription of antimicrobials for an infection that does not need antimicrobial treatment. However, prescription of antibiotics as part of a pre-operative procedure was not considered inappropriate.

(ii) Inappropriate choice: including an inappropriate spectrum of the antimicrobial agent (too broad, too narrow, not effective) or inappropriate toxicity profile.

(iii) Inappropriate application: including inappropriate dosage, timing, route of administration or duration of therapy.

(iv) Appropriate decisions: all criteria of correct antimicrobial use are fulfilled.

(v) Missing or insufficient data to judge the appropriateness of antimicrobial use.

(vi) Any other divergence from departmental antimicrobial policy.

At the end of the pre-intervention period, a preliminary data analysis was conducted to determine the proportion of antimicrobials that were inappropriately prescribed as per the pre-defined analytical plan.

2.5.2. Intervention phase

This phase was carried out for a period of 2 months (December 2017–January 2018) soon after the preliminary results of the pre-intervention phase were available. Three main core intervention strategies (Fig. 1) were implemented.

(i) **Concurrent audit with intervention and feedback:** concurrent audit of antimicrobial use along with direct interaction and feedback with resident doctors was done by the principal investigator (MV) along with the co-investigators. In case the prescription was found to be inappropriate, the treating residents were then informed by the principal investigator, either telephonically or in person, and the reasons were also discussed, whilst the

decision to change those prescriptions were left to the discretion of the consultant in charge.

(ii) **Restriction on antibacterial usage:** residents could not prescribe all antimicrobials by themselves. There was an obligation for residents to seek prior approval from a senior consultant for the prescription of certain higher antimicrobials (carbapenems, polymyxins, linezolid).

(iii) **Education and sensitisation activities:** these activities involved the residents and nurses working in the trauma centre. The aim was to influence their prescribing behaviour and to increase the acceptance of stewardship strategies. The results of the pre-intervention phase were disseminated and discussed with residents from the Department of Orthopaedics in small groups during their bedside rounds as well as with the nurses. Educational materials were posted on notice boards and other prominent places that talked about the rational use of antimicrobials in accordance with departmental antimicrobial guidelines. Daily bedside review of prescription and discussion of the results obtained from the concurrent audit was also done by a consultant from the Department of Orthopaedics. Systematic evaluation of ongoing treatment after a fixed period of initial treatment (i.e. 'antimicrobial time out' after 48 h) was also demonstrated to the residents to avoid redundant antimicrobial use. In case of unavailability of the consultant, cases were discussed on the subsequent working day. The nurses were also sensitised to review antimicrobial prescriptions in terms of their dose, duration and route and to discuss with the treating physician. The following actionable points were considered and prioritised.

(a) **Compliance with departmental antimicrobial policy:** emphasis was placed on prescribing antimicrobials according to the existing departmental antimicrobial policy (Table 1). This policy was displayed at prominent places such as the nursing station, minor operation theatres and near patients' beds. Nurses were casually questioned and then taught about the policy. This helped in keeping a check on unnecessary antimicrobial use as they started questioning usage beyond a period mentioned in the policy.

(b) **De-escalation of therapy:** de-escalation of empirical antimicrobial therapy whenever and wherever applicable on the basis of culture and drug susceptibility testing (CDST) results, and change of redundant combination therapy that can help in eliminating the causative pathogen more effectively.

(c) **Dose optimisation:** Optimisation of antimicrobial dosing was done based on individual patient characteristics (weight, age, liver and kidney function tests), injury pattern, causative organism, site of infection, and pharmacokinetic/pharmacodynamic characteristics of the drug.

(d) **Curb on combination therapy:** routine use of combination therapy to prevent the emergence of resistance is not supported by the existing literature. Therefore, combination therapy that does not have a role in a particular clinical context was not promoted.

(e) **Change in the route of drug administration:** change from parenteral to oral for antimicrobials with good bioavailability was considered when the patient's condition was deemed fit. This was done in compliance with the existing departmental guidelines.

Data were extracted from the patient case files into a data collection tool, the same tool that was used during the pre-intervention phase. Antimicrobial usage was compared across the phases and relevant recommendations were provided to the care providers posted in the ATC.

2.6. Identification of challenges in implementation of the antimicrobial stewardship programme

Weekly meetings were organised by the principal investigator with the co-investigators from the institution to discuss the

Table 1
Antimicrobial policy in the Department of Orthopaedics of the Advanced Trauma Centre, Postgraduate Institute of Medical Education and Research (PGIMER) (Chandigarh, India).

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Closed fractures/ arthroplasty cases	One pre-operative dose of i.v. cephalosporin followed by a single dose intra-operatively and postoperatively. Then, i.v. cephalosporin + amikacin for 3 days, followed by oral cephalosporin for 5 days
Arthroscopy cases	One pre-operative dose of i.v. cephalosporin followed by an intra-operative and postoperative dose for 1 day and orally for 2 days
Open fractures	
(a) Grade I fractures	i.v. cephalosporin from the time of presentation, followed by i.v. cephalosporin + amikacin for 3 days postoperatively, and oral cephalosporin for 5 days subsequently
(b) Grade II open fractures	i.v. cephalosporin + amikacin from the time of presentation until Day 3 postoperatively, followed by oral cephalosporin for 5 days subsequently
(c) Grade III fractures	i.v. cephalosporin + amikacin + metronidazole from the time of presentation until postoperative Day 5, followed by oral cephalosporin until wound healing

i.v., intravenous.
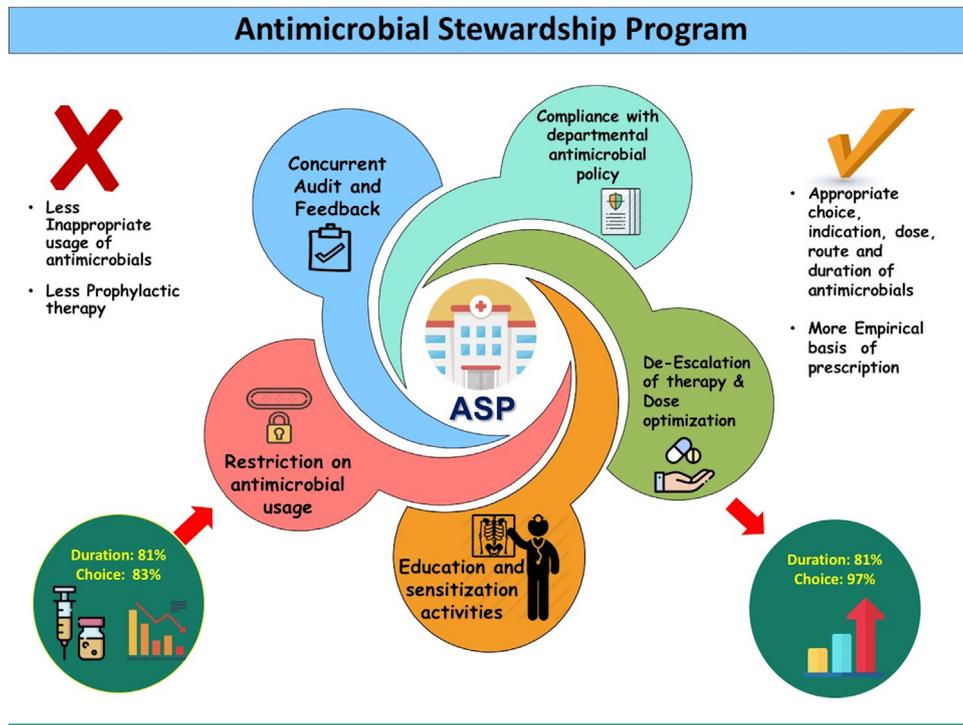
Fig. 1. Main intervention strategies adhered to during the antimicrobial stewardship programme (APS) intervention among patients admitted to a trauma centre of a tertiary care hospital in Chandigarh, India, 2017–2018.

progress of the ASP. Apart from the implementation strategies, various problems encountered during implementation of the ASP in the previous week were discussed, and challenges were documented in the minutes of the meetings. Possible solutions were also brainstormed.

2.7. Data variables, data sources and data collection

The main source of data was inpatient case files for variables such as patient sociodemographic characteristics (age and sex), type of injury, length of hospitalisation, prescription of antimicrobials, name, class, dose, route and frequency of administration of antimicrobials, any adverse drug reactions and CDST results. Other derived variables such as appropriateness of the drug, inappropriate indication, dose, choice of drug and duration were assessed by the expert committee after carefully reviewing the data.

2.8. Statistical analysis

Quantitative data were double-entered, validated and analysed using EpiData v.3.1 for entry and EpiData v.2.2.2.182 for analysis (EpiData Association, Odense, Denmark). The key outcome of the study was the number and proportion of prescriptions with inappropriate antimicrobials and has been summarised using proportions. Antimicrobial usage-related indicators were compared before and after the intervention using a χ^2 test. Logistic regression was performed to determine the association of the intervention with appropriate antibiotic use after adjusting for potential confounders such as age group, sex, place of residence, socioeconomic status, likelihood of infection, time to reach hospital (in days) and duration of hospital stay (in days). The strength of the association was presented as an adjusted odds ratio (aOR). Patient-level clustering was also accounted for in the analysis. Analysis was carried out using the Complex Samples function in IBM SPSS Statistics.

2.9. Ethical approval

Ethical approval was obtained from the Institutional Ethics Committee of PGIMER (Chandigarh, India) and the Ethics Advisory Group of the International Union Against Tuberculosis and Lung Disease (Paris, France). Written informed consent was obtained from the patients or their relatives/attendants before collecting the data. In instances where inappropriate drug prescriptions were observed, the treating resident and the faculty in charge of the unit were immediately informed.

3. Results

Of a total of 748 patients who were admitted to the trauma centre, 695 were admitted for >24 h and were enrolled in the study. The majority of patients were male (587; 84.5%), aged 15–44 years (433; 62.3%), resided in rural areas (405; 58.3%) and belonged to the middle class (450; 64.7%). History of drug allergy was undocumented in 567 patients (81.6%). Most of the patients had bone fractures or joint dislocations (538; 77.4%), and the likelihood of having an infection was considered high in nearly one-half of the patients (319; 45.9%). Sex, place of residence, socioeconomic status and nature of the injury were significantly different between the intervention and pre-intervention groups. A high likelihood of infection (47.7% vs. 42.6%) and cases of bone fracture and joint dislocations (83.7% vs. 65.7%) were more common in the intervention phase compared with the pre-intervention phase. The intervention group also had more patients from rural areas (66%) compared with the pre-intervention phase (43.4%) (Table 2). The immediate outcome of the patients was similar in both groups, except that the proportion of patients who left against medical advice was higher in the intervention phase (3.1% vs. 1.2%). There was no significant difference in the median time to reach hospital or the total duration of stay in hospital in both phases, but the time to operation after injury was significantly reduced in the intervention phase.

Table 2
Sociodemographic and clinical characteristics of patients admitted to the trauma centre of a tertiary care hospital in Chandigarh, India, 2017–2018.[a]

Characteristic	Total	Pre-intervention phase	Intervention phase	P-value
Admitted patients	695 (100)	242 (100)	453 (100)	
Sex				0.004[*]
Male	587 (84.5)	191 (78.9)	396 (87.4)	
Female	108 (15.5)	51 (21.1)	57 (12.6)	
Age group				0.3
≤14 years	56 (8.1)	16 (6.6)	40 (8.8)	
15–44 years	433 (62.3)	158 (65.3)	275 (60.7)	
45–64 years	146 (21.0)	52 (21.5)	94 (20.8)	
≥65 years	60 (8.6)	16 (6.6)	44 (9.7)	
Residence				<0.001[*]
Urban	284 (40.9)	136 (56.2)	148 (32.7)	
Rural	405 (58.3)	105 (43.4)	300 (66.2)	
Not recorded	6 (0.9)	1 (0.4)	5 (1.1)	
Socioeconomic status[b]				<0.001[*]
Lower class	182 (26.2)	88 (36.4)	94 (20.8)	
Middle class	450 (64.7)	138 (57.0)	312 (68.9)	
Upper class	58 (8.3)	16 (6.6)	42 (9.3)	
Not recorded	5 (0.7)	0 (0)	5 (1.1)	
Nature of injury				0.001[*]
Bone fractures/joint dislocations	538 (77.4)	159 (65.7)	379 (83.7)	
Soft tissue injuries	18 (2.6)	11 (4.5)	7 (1.5)	
Multiple injuries	139 (20.0)	72 (29.8)	67 (14.8)	
Likelihood of infection				0.10
Minimal	291 (41.9)	96 (39.7)	195 (43.0)	
Probable	78 (11.2)	39 (16.1)	39 (8.6)	
High	319 (45.9)	103 (42.6)	216 (47.7)	
Could not be assessed	7 (1.0)	4 (1.7)	3 (0.7)	
History of known allergy to any therapeutic drug				<0.001[*]
Yes	6 (0.9)	1 (0.4)	5 (1.1)	
No	122 (17.6)	11 (4.5)	111 (24.5)	
Not documented	567 (81.6)	230 (95.0)	337 (74.4)	
Presence of co-morbidities				0.4
Diabetes mellitus	46 (6.6)	13 (5.4)	33 (7.3)	
Cardiovascular diseases	102 (14.7)	19 (7.9)	83 (18.3)	
Others	39 (5.6)	9 (3.7)	30 (6.6)	
Outcome observed				
Discharge	650 (93.5)	225 (93.0)	425 (93.8)	
Admitted to different ward	20 (2.9)	12 (5.0)	8 (1.8)	0.04[*]
Death	8 (1.2)	2 (0.8)	6 (1.3)	
Left against medical advice	17 (2.4)	3 (1.2)	14 (3.1)	
Time to reach trauma centre after injury (days) [median (IQR)]	1 (1–2)	1 (1–3)	1 (1–2)	0.15
Time to surgery after injury (days) [median (IQR)]	2 (1–4)	3 (1–5)	2 (1–3)	0.02[*]
Duration of hospital stay (days) [median (IQR)]	7 (4–12)	4 (7–11)	8 (4–13)	0.15

IQR, interquartile range.
[a] Data are *n* (%) unless otherwise stated.
[b] Socio-economic status was assessed using the BG Prasad scale.
[*] *P* < 0.05 was considered statistically significant.

A total of 1331 antimicrobials were prescribed (460 in the pre-intervention phase and 871 in the intervention phase). The most common antimicrobials prescribed were cephalosporins (42.6%), aminoglycosides (31.5%) and metronidazole (18.4%). The antimicrobial combinations piperacillin/tazobactam and amoxicillin/clavulanic acid were prescribed for 2.5% and 0.9% of cases respectively. Seven patients (1.0%) received colistin for definitive treatment of hospital-acquired infection due to multidrug-resistant pathogens (data not shown). The duration of stay in this subgroup of seven patients ranged from 34–45 days, they underwent multiple surgeries and received six to seven antibiotics during their hospital stay. The pattern of antimicrobial usage was similar both in the pre-intervention and intervention phases. Use of empirical antimicrobial therapy increased significantly (17.5% vs. 7.4%; *P* < 0.001) during the intervention phase owing to a higher number of cases with a high likelihood of infection (Table 2). The number of patients receiving treatment based on CDST results increased (1.3% vs. 2.3%), while prophylactic therapy decreased significantly (91.3% vs. 80.3%; *P* < 0.001) during the intervention phase (Table 3).

Of the 695 patients, 81.8% and 84.8% were prescribed antimicrobials in the pre-intervention and intervention phases,

respectively (*P* = 0.315). Of the 1331 antimicrobial prescriptions, there was a significant increase in the appropriateness of the duration (81.3% vs. 89.2%; *P* < 0.001), choice (82.8% vs. 96.36%; *P* < 0.001), indication (98.7% vs. 100%; *P* = 0.002) and route of administration (89.1% vs. 97.7%; *P* < 0.001) of antimicrobials during the intervention phase compared with the pre-intervention phase (Table 4). There was no change in the median number of antimicrobials prescribed (2; interquartile range 1–3).

Logistic regression showed that patients in the intervention arm had a significantly higher likelihood of receiving antimicrobials for an appropriate duration [aOR = 2.1, 95% confidence interval (CI) 1.3–3.6; *P* = 0.004] and appropriate reason, i.e. either empirical or laboratory-based rather than prophylactic prescription (aOR = 2.4, 95% CI 1.3–4.3; *P* = 0.003) compared with those in the pre-intervention arm (Table 5). Various challenges that were identified during the intervention phase as well as their possible solutions are shown in Table 6.

4. Discussion

This is one of the few interventional studies of an ASP reported from a trauma centre of a resource-compromised public tertiary

Table 3
Pattern and reasons for antimicrobial prescription during the pre-intervention and intervention phases among patients admitted to a trauma centre of a tertiary care hospital in Chandigarh, India, 2017–2018.[a]

Characteristic	Total	Pre-intervention phase	Intervention phase	P-value
Antimicrobials prescribed	1331 (100)	460 (100)	871 (100)	
Class of antimicrobials prescribed				
Cephalosporins	567 (42.6)	193 (42.0)	374 (42.9)	0.145
Aminoglycosides	419 (31.5)	151 (32.8)	268 (30.8)	0.243
Metronidazole	245 (18.4)	90 (19.6)	155 (17.8)	0.401
Piperacillin/ tazobactam	33 (2.5)	7 (1.5)	26 (3.0)	0.177
Amoxicillin/ clavulanic acid	12 (0.9)	5 (1.1)	7 (0.8)	0.455
Others	55 (4.1)	14 (3.0)	41 (4.7)	0.214
Samples sent for antimicrobial CDST[b]	54/695 (7.8)	18/242 (7.4)	36/453 (7.9)	0.811
Reason for antimicrobial prescription				
Empirical therapy	186 (14.0)	34 (7.4)	152 (17.5)	<0.001[*]
Prophylaxis	1119 (84.1)	420 (91.3)	699 (80.3)	<0.001[*]
Based on CDST report	26 (2.0)	6 (1.3)	20 (2.3)	0.214

CDST, culture and drug susceptibility testing.
[a] Data are *n* (%).
[b] Out of total number of samples in each group.
[*] *P* < 0.05 was considered statistically significant.

Table 4
Appropriateness of antimicrobial prescription during the pre-intervention and intervention phases among patients admitted to a trauma centre of a tertiary care hospital in Chandigarh, India, 2017–2018.[a]

Characteristic	Pre-intervention phase	Intervention phase	P-value
Admitted patients	242 (100)	453 (100)	
Patients on antimicrobial therapy	198 (81.8)	384 (84.8)	0.315
No. of antimicrobial prescriptions	460 (100)	871 (100)	
Appropriate duration	374 (81.3)	777 (89.2)	<0.001[*]
Appropriate choice	381 (82.8)	841 (96.6)	<0.001[*]
Appropriate dose	456 (99.1)	864 (99.2)	0.900
Appropriate indication	454 (98.7)	871 (100)	0.002[*]
Appropriate route	410 (89.1)	851 (97.7)	<0.001[*]

[a] Data are *n* (%).
[*] *P* < 0.05 was considered statistically significant.

Table 5
Association of the antimicrobial stewardship programme intervention with appropriate antibiotic use after adjusting for potential confounders among patients admitted to a trauma centre of a tertiary care hospital in Chandigarh, India, 2017–2018 (*n* = 1443).

Indicator of appropriateness of antibiotic use	aOR (95% CI)	P-value
Appropriate duration	2.1 (1.3–3.6)	0.004
Appropriate route	1.5 (0.6–3.6)	0.3
Appropriate dosage	0.5 (0.2–1.9)	0.3
Appropriate choice	1.7 (0.8–3.4)	0.14
Appropriate reason	2.4 (1.3–4.3)	0.003

aOR, adjusted odds ratio; CI, confidence interval.
Model for appropriate indication was not run because of very few events in one arm of the outcome variable; model is adjusted for age group, sex, place of residence, socioeconomic status, likelihood of infection, time to reach hospital (days), duration of hospital stay (days); analysis was adjusted for patient-level clustering.

Table 6
Challenges faced during implementation of the antimicrobial stewardship programme, with possible solutions.

Challenge identified	Possible solution(s) suggested
Challenges in real-time data capture and abstracting information from patient files	Electronic patient record system
Inadequate orientation of treating doctors to principles of rational antimicrobial use, frequent rotation of residents in the trauma centre	Regular orientation of resident doctors by consultants of the trauma centre, and induction training and sensitisation regarding antimicrobial prescription whenever a new resident is posted. Development of simple training modules for residents as well as nurses
Inadequate involvement of nursing staff in infection control practices	Training of nurses regarding rational antibiotic prescription, infection control practices and supervising review times. Giving more roles to nurses in antibiotic usage guidelines. Upgrading existing pharmacies for catering to the needs of admitted patients
Lack of in-hospital pharmacy	An in-hospital pharmacy enables capturing of data and feedback, ensuring optimised dosing and implementation of front-end practices such as formulary restriction
Long waiting time for CDST reporting	Better communication mechanism between the microbiologist and the treating physician regarding the growth of an organism in the shortest possible time until full culture and susceptibility results become available
Long duration between admission and surgery, and overcrowding in wards	This requires major policy reforms by the hospital administrators to reduce congestion

CDST, culture and drug susceptibility testing.

care hospital in a developing country. The study suggests that ASPs can bring a significant change in appropriate usage of antimicrobials. The predominant change witnessed was the appropriateness of the duration of antimicrobial prescription and reason for prescribing. First, there was a decrease in prophylactic treatment, thus reducing redundant use of antimicrobials. This appears rather contradictory as most patients underwent surgery and did receive prophylactic treatment. However, prescription of antibiotics even when there was no suspicion of infection decreased. Prescription of antimicrobials prophylactically in cases of minimal infection was discouraged by the expert ASP committee and was re-emphasised during the feedback sessions, which might also have resulted in more appropriate indication and less prophylactic use of antimicrobials. Empirical use of antibiotics increased during the intervention phase. This is correlated with an increase in the number of patients who had a higher probability of infection during the intervention phase.

There were significant improvements in patterns of appropriate antimicrobial prescription in terms of duration of use, and choice, indication and route of administration during the intervention phase of the ASP compared with the pre-intervention phase. Switching the route of administration from parenteral to oral as per the treatment guidelines was emphasised during sensitisation activities and concurrent feedback, which might have led to a more appropriate duration and route of administration.

Improvement in the appropriateness of antimicrobial use ranged from 0–14%. In a high patient-load setting, this could translate into benefits for a significant number of patients. This relatively smaller increase in the appropriate use of antimicrobials could be attributed to high baseline values, being a tertiary teaching and research hospital. We speculate that if implemented

in a setting with low baseline values (i.e. low appropriate use of antimicrobials), the intervention would have resulted in much better outcomes. Importantly, an earlier study of prospective audit and feedback in another unit in a similar setting by the antimicrobial stewardship committee brought about considerable improvement in antimicrobial prescriptions [9].

Inappropriate antimicrobial usage is difficult to compare in the scientific literature owing to lack of uniform criteria for judging inappropriateness. However, different studies have reported inappropriate use to range between 9% and 64% [13,15–17]. A systematic review of similar stewardship interventions demonstrated a reduction in excessive use of antimicrobials among hospital inpatients thereby improving clinical outcomes [4].

Many challenges were encountered during the process of implementation of the ASP. Absence of an electronic record system, lack of orientation of treating doctors to principles of rational antimicrobial use, frequent rotation of residents in the trauma centres, inadequate involvement of nursing staff in infection control practices and lack of an in-hospital pharmacy (for enabling formulary restriction and antimicrobial consumption) were several challenges to effective implementation of the ASP that were noted. There were also issues with the hospital governance mechanisms, such as a long waiting time prior to surgery owing to overcrowding, and lack of resources for implementation of infection control leading to a prolonged duration of antimicrobials. Collection of real-time data from patient files and interacting with treating clinicians and the nurses in a busy environment where most patients require immediate attention was another challenge. We were not able to bring a desirable change in prescription practices based on CDST reports. This is probably because the process of sample collection, testing and results took ca. 3–4 days whereas most of the patients who were admitted in the trauma centre generally got transferred out or discharged within 4 days, leading to loss to follow-up of these CDST reports. There is scope for improvement with regard to improving the turnaround time for CDST reporting. Some solutions have also been suggested by the expert committee that need to be taken up by the hospital administration.

One of the strengths of this study was the use of the algorithm of Gyssens et al. [13], which is a reliable method to assess the appropriateness of antimicrobials. A comprehensive multidisciplinary dedicated team of investigators implemented the intervention with the involvement of each concerned department, which found support among the clinicians posted in the trauma centre. There were also several limitations. First, the duration of the intervention phase was relatively short to establish the actual impact of the ASP, although significant changes in practice have been observed. However, the sustainability of the ASP in the long run needs to be judged after a defined follow-up period. Second, it was not possible to assess irrational drug combinations as this was beyond the scope of this study. Third, there were some differences in baseline characteristics of the pre-intervention and intervention arms. However, the differences in these variables were considered as potential confounders and were adjusted in the regression analysis. Future studies can explore the possible fiscal benefits as a consequence of such interventions.

The study results may drive certain key policy implications in hospital settings. Given its effect on the appropriateness of antimicrobial use, the ASP could be replicated in other units of the hospital. ASPs will help provide comprehensive data pertaining to the pattern of drug usage and thus feed into the existing institutional antimicrobial policy. Clinicians involved in patient care must receive regular training on rational antimicrobial prescription practices and be sensitised about the negative long-term sequelae of antimicrobial resistance.

5. Conclusions

The ASP demonstrated significant improvements in the appropriateness of antimicrobial usage. We recommend ASPs in other units of the hospital with adequate institutional support to reduce redundant use of antimicrobials. The Government of India should consider drawing up a policy to implement ASPs at all tertiary care hospitals in the country.

Competing interests

None declared.

Ethical approval

The study protocol was approved by the Institutional Ethics Committee of the Post Graduate Institute of Medical Education and Research (PGIMER) (Chandigarh, India) [approval no. INT/IEC/2017/1319] and the Ethics Advisory Group of the International Union Against Tuberculosis and Lung Disease (Paris, France) [EAG No: 93/17]. Written informed consent was obtained from all of the subjects.

Availability of data and material

The data sets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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