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Retrospective Evaluation of an Antimicrobial Stewardship Program in a Tertiary Care Hospital: A Pharmacist's Perspective

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Abstract:

Objective: This study aimed to evaluate the impact of antimicrobial stewardship (AMS) programs by analysing the dose appropriateness, antibiotic consumption, surgical prophylaxis compliance, drug selection, and de-escalation of antibiotic therapy based on culture and sensitivity reports.

Material and Methods: A retrospective evaluation of data from medical records and antibiotic consumption in the departments of medicine, surgery, paediatrics, and orthopaedics at a tertiary care hospital from November 2021 to February 2022 was conducted. Through coding, the data entered on the pre-designed proforma were converted into statistical variables.

Results: Total overall consumption, daily defined dose, of antibiotics decreased from 412.49 grams (g) to 391.60 g (p-value=0.540, confidence interval [CI]=-10.12–17.08). The percentage of antibiotics prescribed was reduced from 61% to 58%, the average duration of antibiotics per patient was reduced from 4.3 days to 3.7 days, and days of therapy was reduced from 399 to 302 (p-value≤0.001, CI=-465.57–353.24). The time compliance of surgical antibiotic prophylaxis was improved from 95.65% to 99.09% (p-value=0.063, CI=-5.256–0.256). Periodically updated, cumulative hospital antibiogram and antibiotic treatment guidelines were functional, culture and sensitivity-based dosage adjustments were practised in the facility.

Conclusion: A well-run AMS program helps hospitals in promoting compliance with antibiotic prescribing guidelines, preventing antimicrobial resistance by decreasing unnecessary antibiotic use.

Keywords: antimicrobial resistance, antimicrobial stewardship, culture and sensitivity, de-escalation, surgical prophylaxis

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Introduction

Antimicrobial resistance (AMR) is a global health risk associated with the probability of increasing mortality and drug-related toxicity, and it can cause a hike in healthcare expenses. It is known that the misuse and overuse of antibiotics are the driving reason for AMR. As reported in various research studies, 30-50% of antibiotics prescribed for hospital patients are inappropriate or unnecessary for different reasons[1]. With the rapid emergence of resistant pathogens and the current dearth of newer antimicrobials in the research pipeline, it is inevitable to implement steps that ensure appropriate and evidence-based guidelines for the utilisation of antimicrobials to preserve their efficacy. These evidence-based strategies and systematic practices to achieve the above-mentioned goals are collectively referred to as antimicrobial stewardship (AMS) programs. The implementation of these strategies has been recognised as crucial in aiming to rationalise the usage of antibiotics, improve treatment outcomes, limit healthcare-associated infections, AMR, and reduce treatment expenses[2-4]. Moreover, it is also important to conduct a thorough periodic evaluation of the stewardship programs after their implementation in order to acknowledge their impacts and see if further improvements are needed[5,6]. In India, a country with a vast population, a proportionately weak healthcare system, and the risk associated with resistant pathogens like the "ESKAPE" species, the potential of AMR is enormous and serious enough to cause about 10 million deaths annually by 2050[4,7,8].

In this context, our tertiary care centre has implemented stewardship programs, including clinical pharmacist interventions based on the World Health Organization (WHO) AMS programs, aimed at the rational use of antibiotics[9]. Accordingly, the facility established a multidisciplinary AMS team comprising healthcare professionals who possess the necessary expertise, consisting of a physician, a clinical pharmacist, a nurse, and a clinical microbiologist[10,11]. The program implemented in the facility was mainly focused on interventions by clinical pharmacists in cooperation with the AMS team, which included monitoring the dosage appropriateness and antimicrobial consumption (AMC) data, formulating hospital antibiograms, empirical regimens and surgical prophylaxis, framing treatment guidelines, evaluating culture and sensitivity report-based de-escalation and escalation, and switching from intravenous to oral[12,13]. The AMC of the facility was monitored using matrices days of therapy (DOT) and defined daily dose (DDD)[14-16]. The aim of the implemented programs was to increase adherence to the recommended stewardship practices and treatment protocols in order to rationalise the use of antibiotics[17].

This study takes note of the continuing efforts to combat antibiotic resistance, and the efforts put into analysing the various methods in order to improve patient safety by highlighting areas for improvement and intervention. In the study, we aimed to evaluate the impact of the implemented AMS program by analysing the dose appropriateness, consumption and duration of antibiotic therapies, surgical prophylaxis compliance, drug selection and de-escalation based on culture and sensitivity. This evaluation will provide insights into the impact of implementing AMS programs in limiting the misuse of antibiotics using AMC matrices; in turn, it will be useful for comparing drug use patterns between different centres. These periodic evaluations of facility-based AMS programs will also help to generate recommendations for enhancing the effectiveness and sustainability of the AMS program of any healthcare facility.

Material and Methods

A retrospective observational study was conducted in a tertiary hospital using the data of inpatients admitted to the wards of medicine, surgery, pediatrics, and orthopaedics, as these were the departments of the facility where AMS programs were implemented primarily. The study included patient data of all age groups and both sexes who had been hospitalised in the wards and received antibiotic therapy from 1st November 2021 to 28th February 2022. Patients not prescribed antibiotics and with incomplete medical records were excluded from the study. The required data were collected from the medical and laboratory records. Creatinine clearance (CrCl) and dosage adjustments, antibiotic consumption data like DDD and DOT, antibiotic surgical prophylaxis management data, and antibiotic susceptibility testing-based antibiotic therapy data were collected. Specific predesigned data collection forms were used for the data acquisition.

Study procedure

Ethical clearance was received from the Institutional Ethics Committee (Reference no.: ECM PHARM/2021-12). For the retrospective audit, 2 components were employed: level 1, the collection of data from those medical records which were previously recorded during the multidisciplinary ward rounds and from the laboratory data of infectious disease patients, and level 2, the data on the consumption of antibiotics. A work plan was drawn up for the data collection from the medical records of inpatients in the wards of medicine, surgery, pediatrics, and orthopedics. The study intended to analyse the dose appropriateness, consumption and duration of antibiotic therapy, surgical prophylaxis compliance, drug selection and de-escalation based on culture and sensitivity.

Data regarding patient CrCl calculation (COCKCROFT-GAULT FORMULA) and dosage adjustments were collected in order to evaluate pharmacist interventions in dose appropriateness. The antibiotic consumption data used were DDD/100 patient-days, using the aggregated antibiotic dispensing data, including units from the wards. DDD was calculated for each antibiotic separately. The total grams/units administered for each antibiotic dispensed was divided by the WHO-DDD of the antibiotic and multiplied by 100. DOT/1,000 patient-days were calculated based on patient prescription data, regardless of dose or unit administered. DOT was taken as the total number of days of all antibiotics used divided by the number of hospital days, multiplied by 1,000. Surgical patient data were collected in order to evaluate compliance with antibiotics and the timing of surgical prophylaxis therapy to see if they adhered to the guidelines. To evaluate drug selection and optimization, we used data regarding empirical and definitive treatment, escalation, and de-escalation based on culture and sensitivity reports.

Statistical tools

Through coding, the data entered on the pre-designed proforma were converted into statistical variables. The descriptive statistics of the variables are demonstrated as frequency distributions and the demographic profiles are presented as percentages. We examined continuous variables as mean±standard deviation. A paired T-test was carried out to determine the significance of the difference in the DDD, DOT and surgical prophylaxis compliance values between the months studied.

Results

Age-wise CrCl monitored for dosage appropriateness

In all the 366 patients studied, renal function CrCl was monitored for dose appropriateness, and the dosing suggestion was given by the clinical pharmacist if needed.

The age-wise distribution study was done with 4 months of observation. Of the 366 patients monitored for CrCl, 50% (179) were 40–59 years old. Table 1 compares the age distribution of the patients monitored for CrCl from month 1 to month 4. The mean age at 4 months was 61.81±14.38. Table 1 shows the age-wise distribution of patients whose CrCl was monitored for dosage appropriateness (Table 1).

Severity-wise CrCl monitored for dosage appropriateness

A total of 366 patients were monitored for the severity of CrCl. In month 1, of the 13 patients with severe CrCl levels, dosage interventions were made in 8 patients. Followed by month 2, 20 patients had severe CrCl levels, and dosage interventions were done in 4 patients. In month 3, 9 patients had severe creatinine levels. Clinical pharmacist interventions were done in 8 patients, and 6 patients' doses were adjusted. In month 4, 76 patients were monitored, and one patient had severe creatinine levels. In those 9 patients who underwent clinical pharmacist interventions, 4 doses were adjusted (Table 2).

DDD

There was a monthly downward trend in DDD/1,000 inverse to the previous month's antibiotic consumption values. These values were observed to be considerably different each month. Particularly, Piperacillin+Tazobactam was reduced from 83.94 grams (g) in month 1 to 56.2 g in month 4, Cefoperazone+Sulbactam was reduced from 295.16 g to 289.6 g and Meropenem, 25.79 g, to 22.6 g. The DDD values of Colistin, Linezolid, and Teicoplanin usage increased from month 1 to month 4, as the high-end antibiotic usage had increased due to the COVID-19 pandemic situation. The overall consumption of antibiotics at a DDD was reduced from month 1 to month 4 in the study (412.49 g to 391.60 g) (Table 3). However, by conducting a paired T-test, we found no significance in the difference between the DDD values of antibiotics used in month 1 and month 4 (p-value=0.540, confidence interval [CI]=-10.12–17.08).

DOT

In order to know the percentage of antibiotics used, the average number of antibiotics used per patient, and the average duration of antibiotics use, DOT indicators were used. Of the total 3,469 ward admissions in the study period, 2,119 patients had antibiotic prescriptions. On average, 1.5 antibiotics were prescribed for 4.3 days in month 1; likewise, 1.4 antibiotics were prescribed for 4.2 days in month 2, 1.6 antibiotics were prescribed for 3.4 days in month 3, and an average of 1.4 antibiotics for 3.7 days in month 4. The average number of antibiotics prescribed was reduced from month 1 (1.5 drugs) to month 4 (1.4 drugs), and the average duration of antibiotics per patient was reduced from 4.3 days in month 1 to 3.7 days in month 4. The data show that the percentage of antibiotics prescribed was reduced from month 1 (61%) to month 4 (58%). The values of DOT in relation to 1,000 patient-days from month 1 to month 4 were found significant by conducting a paired T-test (p-value≤ 0.001, CI=-465.57–353.24) (Table 4).

Surgical prophylaxis compliance

This study revealed the surgical prophylaxis compliance of 559 patients. For patients who received the appropriate surgical prophylactic antibiotics at the appropriate time, compliance was found correspondingly: month 1=107 (93.04%) and 110 (95.65%), month 2=152 (96.20%) and 156 (98.73%), month 3=170 (96.59%) and 174 (98.86%), and month 4 were 108 (98.18%) and 109 (99.09%). A paired sample T-test was conducted to verify the significance of compliance in surgical prophylaxis timing with the surgeries carried out (p-value=0.063, CI=-5.256 –0.256) (Table 5).

Culture and sensitivity and de-escalation

Microbiology laboratory data were analysed for a total of 188 patients, and the antibiotic susceptibility pattern and cumulative hospital antibiogram were analysed regarding the sensitivity pattern of microorganisms and for empirical therapy suggestions. The hospital cumulative antibiogram, developed by the AMS team based on the facility's antibiotic susceptibility pattern, was not permitted to be published based on the hospital data copyright policy. In the patient data, culture samples were sent if appropriate, and changes in therapy were made based on the report. Considerable cases of de-escalation were done based on the culture and sensitivity reports from high-end antibiotics to lower antibiotics or broad-spectrum to narrow-spectrum antibiotics. Table 6 denotes month wise culture and sensitivity, escalation and de-escalation details (Table 6).

Table 1 Age-wise distribution of patient CrCl monitored for dosage appropriateness

Age (years)	Month 1 (n=77)	Month 2 (n=130)	Month 3 (n=83)	Month 4 (n=76)	Total (n=366) (%)
19-39	8	26	16	24	74 (20)
40-59	44	61	57	17	179 (49)
≥60	25	43	10	35	113 (31)

mean age±S.D.=61.81±14.38

Table 2 Severity-wise distribution of CrCl monitored for dosage adjustment

Months	No. of patients	CrCl (>89)	CrCl mild (60-89)	CrCl moderate (30-59)	CrCl severe (<30)	No of dose changed	Dose not changed
Month 1	77	23	12	19	13	8	2
Month 2	130	19	35	47	20	4	5
Month 3	83	24	31	11	9	6	2
Month 4	76	31	14	21	1	4	5
Total	366	97	92	98	43	22	14

CrCl=creatinine clearance

Table 3 Daily defined dose (Gram) of antibiotics during the implementation of antimicrobial stewardship program

Drug name	DDD value month 1	DDD value month 2	DDD value month 3	DDD value month 4
Meropenem	25.79	26.81	28.77	22.6
Colistin	1.87	5.29	5.86	3.6
Cefoperazone+Sulbactam	295.16	408	355.52	289.6
Piperacillin	83.94	64.74	87.04	56.2
Linezolid	3.86	5.50	6	12.1
Teicoplanin	1.87	7.22	4.59	7.5
Total	412.49	517.56	487.77	391.60

DDD=daily defined dose

Table 4 Days of therapy of antibiotics

Variables	Month 1	Month 2	Month 3	Month 4
No: of patients	778	836	902	953
No: of patients on antibiotics (%)	477 (61)	527 (63)	559 (62)	556 (58)
Average antibiotics per patient	1.5	1.4	1.6	1.4
Average duration of antibiotics (days)	4.3	4.2	3.4	3.7
Days of therapy	399	379	340	302

Table 5 Surgical prophylaxis compliance monitored

Months	No of surgeries	Antibiotic compliance (%)	Time compliance (%)
Month 1	115	107 (93.04)	110 (95.65)
Month 2	158	152 (96.20)	156 (98.73)
Month 3	176	170 (96.59)	174 (98.86)
Month 4	110	108 (98.18)	109 (99.09)

Table 6 Antibiotic monitoring based on culture and sensitivity

Variables	Patients monitored monthly			
	Month 1 (n=44)	Month 2 (n=41)	Month 3 (n=58)	Month 4 (n=45)
Culture/sensitivity test (%)				
Done	40 (90.91)	37 (90.24)	47 (81.03)	40 (88.89)
Not done	4 (9.09)	4 (9.75)	11 (18.97)	5 (11.11)
Culture positive (%)	25 (62.5)	23 (62.16)	29 (61.7)	19 (47.5)
Culture negative (%)	15 (37.5)	14 (37.84)	18 (38.3)	21 (52.5)
Patients on sensitive antibiotics after C&S (%)	17 (42.5)	20 (54.05)	4 (8.51)	4 (10)
Dosage adjustment based on culture report (%)				
Deescalation after C&S	4 (10)	5 (13.51)	0	2 (5)
Escalation after C&S	7 (17.5)	16 (43.24)	0	1 (2.5)
No change	29 (72.5)	16 (43.24)	47 (100)	37 (92.5)

C&S=culture and sensitivity

Discussion

Patients with renal impairment may have altered pharmacokinetic parameters, including medication absorption, protein binding, volume of distribution, and renal excretion. Numerous investigations have demonstrated that individuals with renal impairment frequently experience dosage errors and the possibility of toxicity[18]. Evaluating the dose appropriateness based on renal function is an

important stewardship factor. In the study, a considerable number of patients with seriously impaired renal function underwent interventions with dosage corrections.

DOT and DDD are reliable methods used to calculate the amount of antibiotics consumed. According to the WHO, a drug's DDD is the average maintenance dose given to adults to treat primary indications. The benefit of DDD is its simplicity of computation; it can be applied to cross-hospital or cross-national comparisons[19]. The total number of days the patient receives antibiotic treatment, regardless of dosage or frequency, is known as the "days of therapy". The Infectious Disease Society of America and the Society for Healthcare Epidemiology of America give recommendations using DOT as the criteria for measuring antibiotic consumption[19].

After the implementation and continuous monitoring of AMS programs, there was a monthly downward trend in DDD and DOT, as reported in the results. As the study period was short, the difference between the DDD values during the study period was not statistically significant. However, the overall consumption of antibiotics at a daily defined dose was reduced from month 1 to month 4. The use of DDDs to measure AMC may be challenging as antibiotic dosing varies in infectious disease patients because of the variable pathophysiology of the diseases and patients' hemodynamic status. Moreover, streamlining the use of narrow-spectrum antibiotics may increase DDD-based antibiotic consumption. The DOT values of the study period also showed a reduced trend as an impact of implementing stewardship programs, which was statistically significant. The DOT shows the actual number of days that the antibiotics are used in the wards, whereas DDD is calculated using the average maintenance dose per day for the main indication of the drug, as described by the WHO, which explains the inconsistency found between the significance levels of DDD and DOT. DOT values were found to be reduced due to various factors, such as clinical pharmacist interventions in regulating the duration of therapy, according to renal function and standard treatment guidelines, limiting the appropriate duration of surgical prophylaxis.

Reducing surgical site infection rates and the associated costs is one advantage of assessing how well AMS promotes adherence to surgical antibiotic prophylactic regimes in hospitalised patients. The study results show an increasing compliance rate to both the choice of surgical prophylactic antibiotics and the time of administration from month 1 to month 4. The 3 most important aspects of stewardship programs are "host", "bug", and "drug"; after understanding the host factors, like patient history and clinical characteristics, the presence and characteristics of pathogens need to be identified. Based on the patient's condition, empirical therapy is to be initiated by targeting the possible pathogen and sending culture and sensitivity tests, if found appropriate. De-escalation is a management strategy whereby the spectrum of empirically administered antibiotics is reduced by discontinuing or switching to a narrow-spectrum agent[20]. De-escalation and assessing the appropriateness of antibiotic therapy are 2 critical strategies for optimising the therapy of infected patients while lowering treatment expenses. Appropriate narrow-spectrum antibiotics must be chosen based on the microbiological profile and local antimicrobial susceptibility test reports[21]. This study shows that choosing empirical therapy and de-escalation was considered based on the sensitivity reports and cumulative antibiogram. Observing the inappropriate rate of de-escalations with the increased number of culture-negative cases and subsequent reduction in the number of patients on sensitive antibiotics necessitates further stewardship interventions in this aspect. The rate of de-escalations based on a reduction in culture-positive cases intermittently indicates some prescribers' compliance with

implementing stewardship programs. Even though there are limitations of time lag in reports, selecting the right sample, chances of contamination, specificity and significance of isolates, culture-guided antibiotic therapy remain vital in stewardship programs. Patient management limitations and epidemiological and prescribing uncertainty due to coronavirus disease 2019 (COVID-19) also contributed to the discrepancies in compliance rates with stewardship programs.

Discourse on the strengths of the study: Firstly, there were clear objectives for evaluating the impact of AMS programs in the facility, and clearly defined and quantifiable outcomes based on the WHO-AMS matrices of AMC data, which can be considered as evidence of AMS interventions. Secondly, retrospective observation and data collection were undertaken in a real-world setting directly from hospital records, which may enhance the relevance of the study findings. The notable limitation of the study was certainly its short study period. As the study was carried out during a period when the restrictions as per hospital COVID-19 protocols were operative, the period of data for the study allocated by the authorities was limited. The COVID-19 protocols and associated restrictions in the facility brought about some inappropriate/incomplete data collection in the paediatrics and COVID-19 isolation wards. Furthermore, the data regarding patient comorbidities and severity of illness could not be extracted from medical records for study purposes. Nevertheless, the study's findings on evaluating the impacts of AMS programs may be considered as evidence of advancements and improvements due to these multidisciplinary AMS programs.

Conclusion

It has been noted that implementing AMS program successfully can help reduce irrational antibiotic use and boost compliance with hospital antibiotic prescribing guidelines. Such advancements may aid in limiting the progression of AMR. The study's findings demonstrate that AMS program implementation in a tertiary care centre was linked to important benefits, including compliance with treatment guidelines and limiting unwanted and irrational antimicrobial usage. Evaluation of AMS programs will aid healthcare facilities in framing treatment policies based on the prevalence of pathogens, the detection and control of emerging AMR, framing infection prevention and control policies, the framing of Antibiogram and Standard Treatment Guidelines, and any decisions on AMS upgradations and antibiotic procurement.

Overall, the implementation of the AMS program is clearly strengthened by a multidisciplinary approach with leadership involvement. However, there is still room for improvement in the participation of members like clinical pharmacists and infection control nurses in order to ensure more successful operations of stewardship in the facility.

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Conflict of interest

There are no potential conflicts of interest to declare.

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