Clinical pharmacist-initiated assessment and amelioration of appropriate antibiotic use in surgical units at a South Indian tertiary care hospital - A handshake approach

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Abstract
Introduction: Studies on the appropriateness of antibiotic use among surgical patients are limited in developing countries, notably in India. Therefore, we aimed to evaluate the inappropriateness of antibiotic use, demonstrate the impact of clinical pharmacist interventions and determine the predictors of inappropriate use of antibiotics in the surgical units of a South Indian tertiary care hospital.

Methods: This was a 1-year prospective interventional study on in-patients of the surgical wards to determine the appropriateness of the prescribed antibiotics by reviewing medical records using available antimicrobial susceptibility test reports and medical evidence. When inappropriateness in antibiotic prescriptions was identified, the clinical pharmacist discussed and conveyed apt suggestions to the Surgeon. Bivariate logistic regression analysis was applied to evaluate its predictors.

Results: Among the 660 antibiotic prescriptions of 614 patients that were followed and reviewed, about 64% were inappropriate. Most inappropriate prescriptions were witnessed in the cases that involved the gastrointestinal system (28.03%). Among the inappropriate cases, 35.29% were attributed to an excessive regimen of antibiotic use which marked the highest. Based on the category of use, most of the antibiotics were used inappropriately as prophylaxis (76.7%) followed by empirical (71.31%). The increase in the percentage of the appropriate use of antibiotics resulting from pharmacist intervention was 95.06%. There was a significant link between inappropriate antibiotic use and the presence of two or three comorbid conditions, the use of two antibiotics, and length of hospital stay of 6-10 days and 16-20 days (p < 0.05).

Conclusions: An antibiotic stewardship program in which the Clinical pharmacist is an integral part along with well-framed institutional antibiotic guidelines must be implemented to assure appropriate antibiotic use.

Key words: Antibiotic use; pharmacist intervention; antimicrobial stewardship; clinical pharmacist.


Introduction
Approximately, half to two-thirds of in-patients in hospitals are on antibiotics, and in about 25% to 68% of cases in hospitals, antibiotics are used sub-optimally [1]. About 30%-50% of antibiotics that are prescribed are found to be inappropriate, steering an emergence of resistant bacteria for which the treatment options available are very few, leading to a hike in morbidity, mortality, treatment costs, and adverse drug reactions (ADRs) [2-5]. Approximately, 6.5% of the morbidity and mortality during hospital stays is attributed to inappropriate antibiotic prescribing [6]. An increase in the usage of antibiotics is one of the main contributors to the rise in antibiotic resistance [2,7]. The Centre for Disease Control and Prevention (CDC) estimates that around two million people are infected with drug-resistant bugs annually resulting in approximately 23,000 fatalities [8]. The recent updates estimate that due to antimicrobial resistance (AMR), ten million excess deaths will happen in the coming 30 years [9]. Antibiotic use is prevalent among in-patients in low- and middle-income nations [3]. Therefore, AMR has become a global menace, especially in developing countries like India in the forefront [8]. AMR is on the rise in both hospitals and communities in India mainly due to excessive use and misuse of antibiotics even when it is not necessary [10].

Antibiotics are widely prescribed incorrectly as pre-, peri-, and post-operative prophylaxis with the notion to prevent Surgical Site Infections (SSIs) [11]. It is estimated that antibiotics are used inappropriately in 25 percent to 50 percent of general elective surgeries [12].
In surgical care units, antibiotic resistance leads to longer hospital stays, longer antibiotic therapy, higher mortality, more surgical revisions, and the need for novel antibiotics with increasing toxicity [7]. Therefore, optimizing antibiotic use before, during, and after surgical procedures is essentially urgent for combating AMR and reducing the worldwide burden of illness [13,14].

Clinical pharmacists are known to play a critical role in reducing the burden of AMR by providing real-time interventions that can reduce inappropriate antibiotic use, as well as by assisting other healthcare professionals in optimizing antibiotic use, by providing updated information on antibiotics and ADRs, and by monitoring antibiotic use [15,16]. Collaboration amongst various specialties together as a healthcare team, with the surgeon playing a key role altogether initiating antibiotic stewardship is the most effective method for promoting appropriate antibiotic use in surgical wards [7,14].

However, there is a paucity of research on the appropriateness of antibiotics used as empirical therapy and prophylaxis in surgery units, specifically in developing countries [17]. Also, it is quite noticeable that most of the research conducted was limited to the observational, retrospective, or point-prevalent studies with constricted inclusion criteria that were carried out for a short period which only gives a narrow opportunity for intervention and a mere reflection of clinical practice in the present [1,13,17]. Hence, this study was carried out to understand the extent of the appropriateness of antibiotics used in the surgery wards, documenting how a clinical pharmacist can promote the rational use of antibiotics by interacting with surgeons in real time and determining the predictors of inappropriate use of antibiotics.

**Methodology**

After receiving ethical approval from the Institutional Human Ethics Committee of JSS College of Pharmacy, Mysuru (JSSCPM/ IHEC/ 2019/ 001), this prospective interventional study was carried out by a clinical pharmacist in the surgical units of an 1800-bed multi-speciality tertiary care hospital in South India. All in-patients prescribed with at least one antibiotic between July 2019 and July 2020 were eligible for the study. Patients who had a hospital stay of less than a day were excluded.

All the antibiotic prescriptions of the patients admitted were reviewed daily and those who fit the study criteria were included after receiving their informed consent. The patient demographics, diagnoses, name, dose, dosage form, frequency, duration, indication, and category of use of the antibiotic therapy were recorded. The appropriateness of the prescribed antibiotic was evaluated with internally developed criteria considering the availability of antibiotic susceptibility reports, other lab investigation reports, evidence-based medicine, and credible national and international guidelines to optimize antibiotic regimen concerning dose, frequency, route, and selection of the right antibiotic for the disease state.

When inappropriateness in antibiotic use was identified by the clinical pharmacist, it was conveyed and discussed in person with the concerned healthcare provider and recommendations were made regarding the therapy.

The predictors of inappropriateness associated with antibiotic use were identified at a p value of < 0.05. Using SPSS version 21.0, a bivariate logistic regression analysis was done to determine the p value for categorical variables.

**Results**

During the course of one year, a total of 1266 patients were admitted to the general surgery ward. Among them, 614 patients were enrolled in the study as per the inclusion criteria, 396 (64.49%) of the included patients were male and 218 (35.51 %) were female.

An overall of 1085 antibiotics were prescribed for 614 patients, out of which 601(97.89%) patients were prescribed antibiotics on admission, while 13 (2.11%) patients were already prescribed antibiotics when admitted to the ward. During the study period, 49.84% of patients were administered at least one antibiotic.

Figure 1. Classes of antibiotics prescribed in the study population.
Most of the antibiotics were administered intravenously (96.13%). The incidence of antibiotic use in the general surgical ward during this period was determined to be 48.5% of all reviewed prescriptions.

Out of the total, 58.96% of patients had undergone surgery. Of 1085 antibiotics prescribed, 47% were administered as prophylaxis followed by empirical therapy (44%) and definitive therapy (9%).

Beta-lactam antibiotics (70.6%) were most commonly prescribed in the study population. Among the beta-lactam antibiotics prescribed, the cephalosporin class was frequently prescribed. Details of various classes of antibiotics prescribed are as given in Figure 1.

In 64% of the cases, antibiotics prescribed for the study population were found to be inappropriate. The highest cases of inappropriate antibiotic use (28.03%) involved the gastrointestinal system. On the whole, among the cases in which antibiotics were used inappropriately, the majority \([n = 150 (35.29\%)]\) was an excessive regimen of antibiotics. Overall, Metronidazole \([n = 110 \ (25.8\%)]\) was used inappropriately which was followed by Cefuroxime + sulbactam \([n = 63 \ (14.82\%)]\). Based on the category of use, it was found that 76.7% of antibiotics used as prophylaxis was inappropriate and 71.31% of antibiotics were used inappropriately as empirical therapy. The details of the inappropriate antibiotic use in the study population and the categories of inappropriateness in antibiotic use are summarized in Table 1 and Table 2.

Out of the 660 prescriptions reviewed, 235 prescriptions were found to be appropriate and were considered the control group. Bivariate logistic regression analysis was applied to evaluate the predictors related to inappropriate antibiotic use. Age, gender, comorbid conditions, length of stay, and the number of antibiotics were the parameters considered for assessing predictors. Among them, 2 and 3 comorbid conditions, usage of 2 antibiotics, 6-10 days, and 16-20 days of the length of stay were found to have significance \((p < 0.05)\). The details of predictors associated with the inappropriate use of antibiotics are depicted in Table 3.

A total of 404 suggestions were provided for the cases where inappropriate antibiotic use was identified by the intervening pharmacist. The most frequent suggestion provided was drug withdrawal \([n = 211, \ (52.22\%)]\) while the suggestion for intravenous to oral conversion \([n = 21, \ (5.19\%)]\) was the least. Various suggestions provided by the intervening pharmacist are summarized in Figure 2.

### Table 1. Details of Inappropriate antibiotic use.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. of cases (n = 660)</th>
<th>Appropriate (%)</th>
<th>Inappropriate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal system</td>
<td>338</td>
<td>153 (23.18)</td>
<td>185 (28.03)</td>
</tr>
<tr>
<td>Soft tissue and skin</td>
<td>196</td>
<td>30 (4.54)</td>
<td>166 (25.15)</td>
</tr>
<tr>
<td>Genitourinary system</td>
<td>26</td>
<td>09 (1.36)</td>
<td>17 (2.57)</td>
</tr>
<tr>
<td>Circulatory system</td>
<td>58</td>
<td>28 (4.24)</td>
<td>30 (4.54)</td>
</tr>
<tr>
<td>Endocrine system</td>
<td>14</td>
<td>6 (0.9)</td>
<td>08 (1.21)</td>
</tr>
<tr>
<td>Reproductive system</td>
<td>02</td>
<td>01 (0.15)</td>
<td>01 (0.15)</td>
</tr>
<tr>
<td>Haematological system</td>
<td>11</td>
<td>4 (0.6)</td>
<td>07 (1.06)</td>
</tr>
<tr>
<td>Respiratory system</td>
<td>07</td>
<td>2 (0.3)</td>
<td>05 (0.75)</td>
</tr>
<tr>
<td>Neoplasm</td>
<td>08</td>
<td>2 (0.3)</td>
<td>06 (0.9)</td>
</tr>
</tbody>
</table>

**Category of use**

<table>
<thead>
<tr>
<th>Category of use</th>
<th>No. of antibiotics (n = 1085)</th>
<th>Appropriate (%)</th>
<th>Inappropriate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prophylaxis</td>
<td>508</td>
<td>118 (23.22)</td>
<td>390 (76.77)</td>
</tr>
<tr>
<td>Empirical</td>
<td>481</td>
<td>138 (28.69)</td>
<td>343 (71.31)</td>
</tr>
<tr>
<td>Definitive</td>
<td>96</td>
<td>96 (8.84)</td>
<td>--</td>
</tr>
</tbody>
</table>

* Few patients may have presented with more than one diagnosis.

### Table 2. Categories of the inappropriateness in antibiotic use.

<table>
<thead>
<tr>
<th>Categories of Inappropriateness</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regimen excessive</td>
<td>150 (35.29)</td>
</tr>
<tr>
<td>Regimen inadequate</td>
<td>103 (24.24)</td>
</tr>
<tr>
<td>Inappropriate selection</td>
<td>63 (14.82)</td>
</tr>
<tr>
<td>Antibiotic given without indication</td>
<td>58 (13.65)</td>
</tr>
<tr>
<td>Similar spectrum of activity</td>
<td>51 (12)</td>
</tr>
</tbody>
</table>

### Discussion

To our knowledge, this is the first study of its kind to investigate the appropriateness of antibiotic therapy and predictors associated with inappropriate antibiotic therapy among surgical patients in India. The impact of clinical pharmacist interventions in improving antibiotic use

- Number of cases in which antibiotics were used inappropriately = 425
- Number of clinical pharmacist’s contributions resulting in appropriate antibiotic use = 404
- Percentage increase in the appropriate use of antibiotics resulting from pharmacist intervention = \(404 / 425 \times 100 = 95.06\%\)

* Few patients may have presented with more than one diagnosis.
appropriate use of antibiotics can help in preventing adverse drug reactions, AMR, morbidity, and mortality and bring down healthcare costs [3,5,7,8,14]. This study identified that around 48.4% of the inpatients in surgery wards were on antibiotic therapy. Here, in 64% of cases, antibiotics were prescribed inappropriately. In contrast to this, 70.3% of inappropriateness was observed in a study conducted in Pakistan, while it was comparable to the findings of studies in Europe (65%-69.9%) [3,18]. It differed from the study results in Ethiopia (30.9%) and Switzerland (33%). In this study, it was found that the rate of inappropriateness was high with antibiotic prescriptions used for prophylaxis which was unlike the findings in another study conducted in Switzerland (37%) [19]. This could be because our study was exclusively carried out in surgical units and most of the patients underwent surgeries and therefore had to be initiated with prophylaxis before surgery.

Among the cases where antibiotics were used inappropriately, 35.29% of cases were found to have an excessive regimen of antibiotic use, which was mainly due to inappropriate duration of antibiotic therapy, alternative dosage forms, overdose, and use of broad-spectrum antibiotics. Typically, surgical infections are inappropriately managed by administering antibiotics for longer than necessary or by using broad-spectrum antibiotics when a narrower-spectrum agent would be sufficient [20]. Surgeons still believe that prolonged therapy and multiple antibiotics are more effective to prevent SSIs than a narrow-spectrum antibiotic administered for a shorter duration [21]. In our settings, few surgeons relied on broad-spectrum antibiotics as they had an opinion that these could prevent SSIs more effectively than compared to narrow-spectrum antibiotics and so there were many instances in which third-generation cephalosporins were used instead of first/second-generation cephalosporins for surgical prophylaxis for a prolonged period. This was one of the reasons for methicillin-resistant Staphylococcus aureus outbreaks in surgical units [21].

In this study, it was observed that most of the antibiotics were administered intravenously. Such instances may arise due to the unawareness about the spectrum of coverage of antibiotics and beliefs that IV antibiotics may have more bioavailability and efficacy than oral antibiotics also prescribing antibiotics till discharge would improve the patient’s conditions even after the infection resolves. Similar to this study, a study conducted by Taalam et al. showed that improper...
duration of therapy (45.9%) was the most common cause of inappropriate antibiotic use during the hospital stay [22]. In contrast to this finding, a study by Amer et al. showed that cases that had adequate regimens for the indication (28.57%) were found to be the major reason for inappropriateness [23]. This difference in findings could be linked to the difference in study sites and the different disease conditions in both studies. Of the 1085 antibiotics prescribed in this study, 47% of antibiotics were administered as prophylaxis. In our study, most of the patients were diagnosed with gastrointestinal (51.21%) and skin and soft tissue (29.7%) related disease conditions, and the majority (58.96%) had undergone surgical procedures. According to the guidelines for surgical prophylaxis, it is recommended that antibiotics should be given 30 to 60 minutes before a surgical incision as prophylaxis [21]. In clean surgeries such as surgeries performed for skin and soft tissues, first or second-generation cephalosporins should be administered as prophylaxis, whereas in surgical procedures related to gastrointestinal disease conditions (clean-contaminated and contaminated cases), first or second-generation cephalosporin along with a nitroimidazole is to be administered [24]. But it was seen that the prophylactic therapy was continued post-procedure even if the patient was clinically stable. Increased and prolonged use of antibiotics as prophylaxis was mostly due to the thought about its action of inhibiting bacterial growth, thus minimizing the risk of surgical site infections. This was probably the reason why Cefuroxime + Sulbactam and Metronidazole were found to be used inappropriately the most.

In contrast to this, the evidence establishes that prophylaxis for a short duration is advised over prophylaxis for a longer duration in preventing SSIs as no additional anti-bacterial benefits were exhibited when prophylaxis was prolonged for more than 24-72 hours and also that similar rates of SSIs were noted with both short duration and prolonged duration of prophylaxis [25].

The inappropriate use of broad-spectrum antibiotics and long duration of antibiotic treatment pose a considerable threat to AMR and Clostridium difficile-associated diarrhea as well [1,7,17,23]. The overuse of metronidazole and third-generation cephalosporins may increase the chances of health-care associated infections such as Vancomycin-resistant Enterococcus infections [26]. It was noted that the carbapenems and glycopeptides were used comparatively less in the surgery wards, which was similar to the results in the study conducted in Ethiopia [5]. In the study conducted in Pakistan, about 88-97.6% of antibiotics were prescribed to patients without performing culture sensitivity tests which were comparable to the findings in our study. Also, it was observed that if ever culture sensitivity tests were done for cases, it was often after initiating empirical therapy. However, cultures collected during antibiotic therapy have been accompanied by a substantial drop in pathogen detection, hence hindering antibiotic optimization and de-escalation [27]. Antibiotic susceptibility tests before therapy are therefore vital as they can aid in minimizing inefficient antibiotic use, ADRs, and AMR [28].

A total of 404 suggestions were provided for the cases where inappropriate antibiotic use was identified by the intervening pharmacist in this study with an acceptance rate of 99%, which was higher than that of a study conducted in Saudi Arabia with an acceptance rate of 96.3%. However, the suggestions provided were similar to that of our study which included drug withdrawal, optimization of antibiotic treatment concerning dose, frequency, and route of administration, and change of antibiotic therapy about the spectrum of coverage [23]. Thus, clinical pharmacists can play an outstanding role in ensuring the quality use of antibiotics through proactive involvement in the healthcare team by interacting with various healthcare professionals in real-time.

Two and three comorbid conditions, two antibiotics, who stayed for 6-10 days, and 16-20 days of LOS were found to be significant predictors (\(p < 0.05\)) associated with inappropriateness. This can be explained concerning the general practice where antibiotic therapy is continued throughout the entire hospital stay in patients with comorbidities like Diabetes mellitus who remain at the hospital for a longer period due to severe soft tissue and skin infections or severe gastrointestinal infections, which were the most common diagnoses in this study. In contrast to this, a study conducted by Atif et al. showed that gender is a significant predictor of inappropriateness [29]. Therefore, understanding predictors can help clinical pharmacists give attention to the patient population at risk of inappropriate antibiotic use to develop preventive strategies.

Our research was able to emphasize the need of initiating an ‘Antibiotic Stewardship Program’ and the extent of necessity for the preparation of a ‘local antibiotic policy’ for clinical practice. As a result, the general surgeons of our hospital were convinced to collaborate with the clinical pharmacist and the Department of Microbiology to frame an Antibiotic Policy for the General Surgery department. The
limitation of the study was that it was carried out only at a single General Surgery department of a tertiary care hospital setting and that the clinical pharmacist was not able to assess the economic impact of the interventions made during this period.

Conclusions

As antibiotics are life-saving drugs that have an important role in managing the severe infections and complications associated with them, strategies should be designed and implemented to rationalize antibiotic use as antibiotic resistance is an arising global crisis. It is very much evident from the study that there is a crucial need for an antibiotic stewardship program to be initiated by developing an institutional antibiotic guideline, thereby encouraging and reinforcing appropriate antibiotic use.

Also, this demonstrates that clinical pharmacists can serve an indispensable role in optimizing antibiotic use by monitoring antibiotic prescriptions for their indication, dose, frequency, route of administration, and duration of therapy by providing their timely suggestions. This could, in turn, reduce the cost of therapy and length of stay at the hospital, occurrence of adverse drug reactions and in the long run, would help in tackling AMR.

References


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