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Study of antibiotic prescribing pattern among hospitalized patients with Systemic Bacterial Infection in a Tertiary Care Hospital of Central India

Swati B Gajbhiye[1], Dilip S Gedam[2*], Madhavi V Madkey[3], Ashish N Meshram[4]

1. Assistant Professor, Department of Microbiology, Government Medical College, Gondia, Maharashtra, India.
2. Professor and Head, Department of Microbiology, Government Medical College, Gondia, Maharashtra, India.
3. Assistant Professor, Department of Microbiology, Government Medical College, Gondia, Maharashtra, India.
4. Senior Technician, Department of Microbiology, Government Medical College, Gondia, Maharashtra, India.

Abstract

***Aim**: The aim of the present study was to perform a systematic and comprehensive assessment of antibiotic use practice in hospitalized patients with systemic bacterial infections to identify institutional targets for better antibiotic and health care resource stewardship. **Material and Methods**: It was institution based prospective observational study conducted from October 2018 to April 2019. Patients with suspected systemic bacterial infections during this period were strictly followed and data was abstracted using data abstraction format. **Results**: Nearly 40% (278/695) of patients had suspected bacterial infection during admission. Pneumonia (48%, 133/278) was the most common. Among 503 antibiotics prescribed; Cephalosporins (38.4.%, 140/364) was most commonly used in wards and Piperacillin+Tazobactum (17.9%,25/139), Cefoperazone+Sulbactum (14.3%, 20/139) were most widely prescribed fixed dose combination (FDC) in ICU. Overall rationality of antibiotics administered was 56.8% and 59.3% antibiotics were found appropriate with indication, 59.3% with duration, 59.07% with dose and 56.31% with frequency. Empiric antibiotic therapy was initiated in 94.6% (229/242) ward and all (36/36) ICU patients while culture sensitivity was conducted for only 23% (64). Appropriate escalation in 27% and de-escaltion in 8.3% to culture sensitivity reports. Antibiotics were not changed in large proportion of cases i.e. in 52% cases. No discontinuation of empiric therapy was performed for negative culture reports considered inappropriate. **Conclusion:** Judicious antimicrobial use through educational and antimicrobial stewardship programs remains critical to control the spread of antibiotic resistance.*

***Keywords**: Antibiotic prescribing pattern, Antimicrobial agents, Systemic bacterial infections*

Address for correspondence: Dr. Dilip S. Gedam. Professor and Head, Department of Microbiology, Government Medical College, Gondia, Maharashtra, India. Contact No: +919403119007. swatilade2306@gmail.com

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Introduction

Irrational antibiotics/antibacterials (ABs) usage is a global problem especially in developing countries resulting in an increased emergence of resistance to most common bacteria, higher cost of treatment, prolonged hospitalization and adverse drug reactions.[1] About half of the antimicrobial agents prescribed to hospital in-patients are considered inappropriate.[2] A myriad of contextual factors may influence antibiotic prescribing including social, institutional, economic, political, and cultural factors warranting development of innovative strategies and interventions.[3] Studies in high income and low and middle income (LMIC) countries have shown that it is often doctor perception of patient demand rather than actual patient demand that is associated with antibiotic over prescription.[4] The recent reports of emergence and importation of novel multidrug-resistant mechanism in bacterial pathogens from India and other countries in South Asia is a serious concern.[5,6]

The prevalent use of antimicrobial agents in India varies from 24 to 67% whereas in developed countries around 30% of the hospitalized patients are treated with these drugs.[7,8] A recent community based surveillance report indicated a much higher use of antimicrobials in three Indian cities compared with two cities in South Africa but also indicated the operational and logistical challenges of long-term surveillance of antimicrobial use in LMIC.[7] One report from two private hospitals in Ujjain, India, demonstrates widespread antibiotic prescribing.[9] Different approaches have been promoted to save these precious drugs from the threat of resistant bacteria selection[10]. Several strategies to optimize the use of antibiotics, often referred to as antibiotic stewardship programs, have been developed. Antimicrobial stewardship is currently considered as the promising approach and has been promoted for all hospitals.[11,12] Monitoring of antimicrobial use and knowledge of prescription habits are some of the strategies recommended to contain resistance to antimicrobials in hospitalized patients.[13] The aim of the present study was therefore to perform a systematic and comprehensive assessment of antibiotic use practice in hospitalized patients with systemic bacterial infections, in order to identify institutional targets for better antibiotic and health care resource stewardship with the goal of identifying gaps and inform interventions that could lead to judicious use of antimicrobials and development of antimicrobial stewardship program.

Materials and Methods

The study was an institution based prospective observational study conducted from October 2018 to April 2019 over a period of consecutive 6 months. A total of 695 patients hospitalized in ward and ICU were included in the study out of which 242 of wards and 36 of ICU patients with suspected systemic bacterial infections were strictly followed for antibiotic prescription pattern using data abstraction format.

Data abstraction format was adopted from different literatures. The data collectors were two microbiologists and one Infection control nurse. To maximize the quality of the data, training, regular supervision and monitoring of the data collectors were performed. Patients who had (on admission) and developed (in the hospital stay) systemic bacterial (except mycobacterial) infections were strictly followed. Demographic characteristics, admission diagnosis, suspected infection diagnosis, multidrug resistance (MDR) risk factors, laboratory procedures performed (culture & gram staining) and the date of each laboratory report were documented properly. In addition, antibiotics administered, follow-up adjustments to the antibiotic regimen, and the dates' of each antibiotic initiation and adjustment were also recorded properly. Criteria's used for diagnosis, the microbiologic techniques, the decision to prescribe and modify antibiotics were left for the physician's discretion. The collected data was analyzed using SPSS software version 21.

Ethical consideration

Ethical approval was obtained from the Ethics committee of Government medical college, Gondia. Since the data collection was primarily dependent on patient charts, no written consent was requested from patients. However, information was given to patients, their physicians, and other health workers, as required. To ensure confidentiality, name and other identifiers of patients and prescribers were not recorded.

Operational definitions

Adjustment: Changes made to the antibiotic/regimen after 48–72 hours of the initial therapy that refers to either of the following:

Discontinued: Meaning discontinuation of all antibiotics found to be unnecessary (e.g. no suspected infection).

Modified: Meaning either de-escalation (narrowing by either discontinuation of either agent or using the narrower spectrum option) or broadening (addition or using a much broader spectrum instead) of therapy.

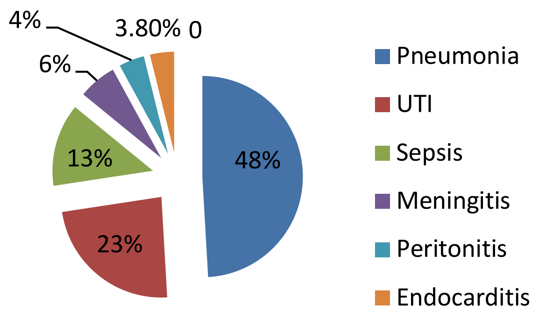
Results

Using the total medicine ward and ICU admissions as the denominator, the systemic bacterial infection rate was 38.65% (242/626) for the wards and 52.17% (36/69) for the ICU.

Overall, 40% (278) of the patients had suspected infection during admissions. Patients with circulatory disease (34.4%) accounted for the second higher category of primary admission diagnosis. Patients had a mean age of 41.8± 17.8 (range: 18–85) and males accounted for about 56% of the study participants.

Of all the patients, 48.0%(133) had pneumonia, 23%(64) had UTI followed by sepsis 13%(36) ,meningitis 6%(17),peritonitis 4%(11) and endocarditis 4%(11) depicted in Fig 1. Community-acquired pneumonia in wards (25.2%) and aspiration pneumonia in ICU (36.6%) were the commonest types of pneumonias suspected. Similarly, among 45%(29) UTI patients, 24% (7) in wards and 34%(10) in ICU were CAUTI.

Fig 1: Distribution of suspected bacterial infections



When grouped in a class comparatively cephalosporin 38.4% (140/364) vs. 28.5% (39/139) followed by anti-anaerobic (6.8% vs. 10.7%) were the prevalently used class of drugs across the settings. As depicted in table 1, the most frequently prescribed antibiotics were (ward vs. ICU) ceftriaxone (25.8% vs. 15.1%%), Piperacillinipe + Tazobactum (9.8%vs 17.9%), Cefoperazone + Sulbactum (11.5% vs 14.3%), metronidazole (6.8% vs. 10.7%%) Cefepime (5.7% vs 3.5%), Amoxycillin+Clavulanic Acid (Augmentin) (10.9% vs 3.5%) and Norfloxacin (6.8% vs 2.8%) Vancomycin (2.1% vs. 7.1%) and Imipenem /Meropenem (1% vs 7.1%) followed by Tigecycline and Collistin were most commonly in ICU as compared to ward.

Other Antibiotics

Wards: Clindamycin (8), Cloxacillin (3), Gemifloxacin (1),Cefotaxime (2), Cephalexin (1), Crystalline penicillin (1), Doxycycline (2), Chloramphenicol (1),Clarithromycin (2), Amoxicillin (2).

ICU:

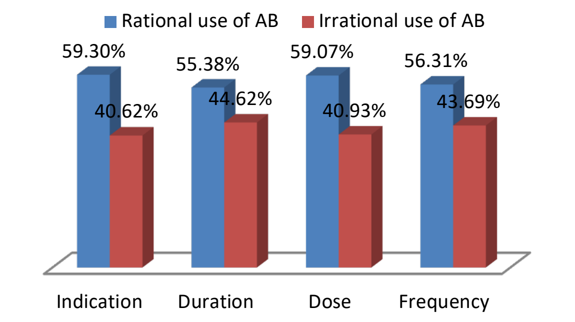
Clindamycin (1), Clarithromycin (1), Tigecycline (2), Colistin (3)

Table 1: Total Antibiotics prescribed in ward and ICU

Antibiotics	Ward (n=364)	ICU (n=139)	Total (n=503)
Ceftriaxone	94(25.8%)	21(15.1%)	115 (22.8%)
Pip+ Tazo	36(9.8%)	25(17.9%)	61 (12.1%)
Cefo. + sulbactum	42(11.5%)	20(14.3%)	62 (12.3%)
Metronidazole	25(6.8 %)	15(10.7%)	40(7.9%)
Ceftazidime	25(6.8%)	13(9.3 %)	38(7.5%)
Augmentin	40 (10.9 %)	5(3.5%)	45 (8.9%)
Vancomycin	8 (2.1 %)	10(7.1 %)	18 (3.5%)
Norfloxacin	25(6.8%)	4 (2.8 %)	29 (5.7%)
Gentamycin/Amikacin	17(4.6 %)	8 (5.7 %)	25(4.9%)
Cefepime	21 (5.7 %)	5(3.5 %)	26 (5.1%)
Imipenem/ Meropenem	4 (1 %)	10(7.1 %)	14 (2.7%)
Others	23(6.3%)	7 (5.0 %)	30 (5.9%)

When rationality was checked for overall appropriateness of antibiotics prescribed it was found to be56.8% (286). It was found that, 59.3% (298) antibiotics were appropriate specially with reference to indication and 59.3% (298) with duration. Similarly, 59.07% (297) with dose, 56.31% (283) with frequency were found to be appropriate and the same is given in the Figure.2

Fig 2: Comparison of appropriateness of antibiotics prescribed in hospitalized patients.



While culture sensitivity was conducted for only 24.1% (64/265). As described in table 2, the antibiotics were modified (either escalated, deescalated or discontinued) in 47.9% cases only as per the culture sensitivity report.

Appropriate escalation in 10.4% in ward vs 20.8% in ICU and de-escalation in 4.16% according to the culture sensitivity reports. The antibiotics were not changed in large proportion of cases i.e in 52% even after the availability of reports. No discontinuation of empiric therapy was performed for negative culture reports (10/16) considered inappropriate.

Table 2: Adjustments to the initial antibiotic therapy for hospitalized patients with systemic bacterial infection

Antibiotic adjustment	Ward		ICU	Total		
Modified – Escalation	5(10.41%)	14.5%	8(16.66%)	20.8%	13(27%)	35.4%
De-escalation	2(4.16%)		2 (4.16%)		4 (8.3%)	
No change	10(20.83%)		15(31.25%)		25(52%)	
Discontinued	4 (8.33%)		2(4.16%)		6(12.5%)	

Discussion

Antibiotic resistance among pathogenic microorganisms is a matter of worldwide concern. Selective pressure by antimicrobial drugs is by far the most important driving force for the development of such resistance. Antibiotics are among the most commonly prescribed drugs in hospitals and in developed countries around 30% of the hospitalized patients are treated with these drugs.In our study, 278 hospitalized Patients with suspected systemic bacterial infections during a period of 6 months were strictly followed for the antimicrobial prescribing pattern using data abstraction format and a total of 503antibiotics were prescribed. There were more male patients as compared to females. This was comparable with previous studies.[14,15] The reason for more male admissions in our study may be that female patients are reluctant to utilize health care facilities unless they are critically ill.

The average age of patients was 44 years and most of the patients were of 30-60 years age group which correlates well with the study conducted in Northern India by Williams et al.[14] Similarly , in a study carried out by Rajalingam *et al;* among 200 patients participated in the study, the age ranged between 15-87 years with an average of 49.25 ± 20.69 years.[16]This is in contradiction with a study carried out by Salman et al and Gafar A et al in their studies reported that majority of students in their studies belong to 20 -30 age group. This was similar to earlier studies where most of the patients in whom antimicrobials were prescribed belonged to 16-30 years of age group.[17,18]

Consistent with a review report in low and middle-income countries, pneumonia was the most common infection in hospitalized patients. This was similar as previous studies indicating that respiratory tract infections dominate amongst all infections.[19,20] In a study carried out at internal medicine ward in 2003 at tertiary care hospital, Nepal, the most common condition for which an antibiotic prescribed was chronic obstructive pulmonary disease in 22.7% followed by lower respiratory tract infections 15.8%, urinary tract infections 13.3% and pneumonia (8.9%)[21]. Further, in a study carried out by Metler et al[22] in 2007 among 297 cases, the most common conditions for antibiotic administration were respiratory tract infections (31.4%).UTI (21.0%), Gastrointestinal infections(15.0%), Skin and soft tissue infections(7.8%) followed by Sepsis(3.2%) and least were Central nervous system infections 2.0%.

In our study, among 278 hospitalized Patients with suspected systemic bacterial infections a total of 503 antibiotics were prescribed. The higher rates of prescribing antibiotics in our institute could be because it is tertiary hospital with most of the critical patients referred from other centers. As intravenous access was there, the in-patients are sick and as most of the available effective antimicrobial antibiotics (AMAs) are available in injection form, most of the AMAs (72.56%) were administered intravenously in this study. Cephalosporins (38.4%,140/364) in wards and Piperacillin+Tazobactum (17.9%,25/139) followed by Cefoperazone+Sulbactum(14.3%, 20/139) were most widely prescribed FDC in ICU.

Badar VA et[13] al in their study from Central India reported cefotaxime (32%) as the most commonly used antimicrobial in 32% followed by metronidazole in 24% and ampicillin in 17.29% hospitalized patients in intensive care unit. B. Rajalingam et al[16] also reported cephalosporins (ceftriaxone 15.38%), followed by quinolones (levofloxacin 6.76%) as the most commonly prescribed drug among the 200 hospitalized patients of Coimbatore.

The commonest antimicrobial in our study was Ceftriaxone; this is in accordance with previous studies, where Ceftriaxone was most commonly prescribed.[23,24] This may be because Cephalosporins are broad spectrum antimicrobials effective against vast majority of organisms, have convenient dosing schedules and have fewer adverse effects; hence they are being prescribed more frequently both in wards and intensive care units. This may be one of the reasons for growing cephalosporin resistance in this region.[25] In fixed dose combinations, the most commonly prescribed antibiotics were cefepime+tazobactum (19.69%) followed by piperacillin+tazobactum (14.76%) specially in ICU. The rationale for combination antimicrobial therapy includes broad-spectrum empirical therapy for serious infections, improved clinical outcomes, and the prevention of resistance. Given the cost of combination therapy, guidelines restrict such treatment approaches for certain group of patients and recommend prompt de-escalation based on the patient's clinical course, and culture & susceptibility test results Despite this concept though majority of our patients started with broad-spectrum combination empiric therapies, the modification was done only for few numberof the patients. Even these modifications did not necessarily indicate streamlining (lowering the estimate) since the majority of the modifications involved the addition of therapy for clinical deterioration, identification of new site of infection, and for culture-positive microbiologic reports.

Empiric antibiotic therapy was initiated in 94.6% (229/242) ward and all (36/36) ICU patients while culture sensitivity was conducted for only 24.1%(64/265). The most commonly used antibiotic for both empirical and adjusted therapy was Broad-spectrum antibiotics ceftriaxone, piperacillin/tazobactam, cefoperazone/ sulbactum, imipenem, meropenem or vancomycin. The empirical therapy was adjusted (either escalation , de-escalation or discontinuation) in 47.9% cases as per the culture sensitivity report. Appropriate escalation done in 10.4% in ward vs 20.8% in ICU and de-escaltion in 4.16% according to the culture sensitivity reports. The antibiotics that were not changed in 52% were considered as inapropriate. Among the total 64 culture reports originated from the ward and ICU; 16 of the available reports were negative and thus susceptibility was done for the 48 of the positive cultures only. Among the 48 positive culture reports; the most common organisms were *Klebsiella pneumoniae* (12 patients, 25%), and *Pseudomonas aeruginosa* (12 patients, 25%) followed by *Escherichia coli* (9 patients, 18.7%), *Staphylococcus aureus* (8 patients, 16.6%), *Acinetobacter baumani* (5 patients, 10.4%) and *Streptococcus pneumoniae* (2 patients, 4.1%). However, the antibiotics were not changed in large proportion of cases 25/48 i.e in 52% as per the culture sensitivity report even after the availability of reports and no discontinuation of the empiric antibiotic therapy was performed for negative culture reports (10/16) thus considered to be inappropriate. The failure to adapt therapy to culture results suggests that microbiological investigations had an insufficient impact on the management of patients. A similar problem was observed in a study, where in 55% of patients with clinically significant culture results and an inappropriate empirical regimen, the medication was not changed to a more appropriate antibiotic[26]. In both empirical and adjusted antibiotic therapy the most common reason for inadequacy was the use of antibiotics with a too broad spectrum. The second most common reason for inadequate adjusted therapy was the use of antibiotics ineffective against isolated pathogenic bacteria or against bacteria to be expected according to the postulated infections, or the continuation of antibiotic therapy even after negative cultures ruled out an infection e.g. in the case of assumed urinary tract infections.

Overall, antibiotic prescribed were rational in 57.85% patients but most of the prescriptions were not supported by culture and sensitivity reports as it was not done in many patients of

ICU. Nearly 60.61% antibiotics were found appropriate with indication, 55.38% with duration, 59.07% with dose and 56.31% with frequency. The results of our study correlates well with a study carried out by *B. Rajalingam*[16] in 200 medicine and pulmonary ward patients reported the overall appropriateness to be 57.85% while Appropriateness of antibiotics for indication was 60.61% and duration was 55.38%, dose (59.07%) and frequency (56.31%). In our study, nearly 42% of antibiotics prescribed were found be inappropriate. In 1998 Kshirsagar MJ et al.[27] reported that more than 30% of medical prescriptions were irrational, with the probability of such prescriptions increasing significantly with the number of drugs per 3 prescriptions. Similarly, Badar VA and Navale SB[13] could find rational use of antimicrobial agents in only 30% patients.

Multidisciplinary development of evidence-based practice guidelines incorporating local microbiology and resistance patterns can improve antimicrobial utilization. The clinical microbiology laboratory plays a critical role in antimicrobial stewardship by providing patient-specific culture and susceptibility data to optimize individual antimicrobial management. Timely and accurate reporting of microbiology susceptibility test results allows selection of more appropriate and focused therapy, and may help reduce broad-spectrum antimicrobial use. Dissemination of antibiograms to clinicians may allow better selection of empirical therapy based on local susceptibility patterns. However, clinicians must be wary of over interpreting results from antibiograms when the absolute number of isolates is very small or when susceptibilities are reported for a specific unit e.g., a single intensive care unit or over a short time period e.g., monthly.

Conclusion

Our observations showed that about half of admitted patients had suspected infection andreceived antibiotics on an empiric basis. Culture sensitivity was conducted for only 24.1%cases (64/265) and among them only 47.9% of the empiric antibiotics were justified based on microbiologic cultures. The proportion of antibiotic use for bacteriologically proven infection was low and efforts to prescribe antibiotics on a sound bacteriological basis should be encouraged.

The rate of inadequate antibiotic therapies was 42% which was similar to the rates reported from other institutions. Surprisingly, adjusted antibiotic therapies were more frequently inappropriate than empirical therapies. Interventions aiming at improving antibiotic prescribing should focus on both initial empirical therapy and streamlining and adjustment of therapy once microbiological results become available.

Addressing prescribing behavior is a key component of antimicrobial stewardship. Formulation of local antibiotic protocol and adherence to the same can improve prescribing pattern and thereby antimicrobial sensitivity.

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