

Original Research Article

Evaluation of restricted antibiotic utilization and cost-minimization analysis in a tertiary care hospital in India

Dhakchinamoorthi Krishna Kumar^{1*}, Mani Swapna², Srinivasan Kanmani³,
Varghese Varsha⁴, Nair V. Vidya⁵

¹Department of Pharmacy Practice/ Clinical Pharmacy, Karpagam College of Pharmacy, Karpagam Medical College & Hospital, Coimbatore, India

²Clinical Pharmacologist, Manipal Hospitals, New Delhi, India

³Regional Project Manager, Servier Pharmaceuticals (India), Chennai, India

⁴Clinical Pharmacist, KIMS Health, Trivandrum, Kerala, India

⁵Pharmacist, DMC Hospital, Thadiyoor, Kerala, India

Received: 11 October 2020

Revised: 02 December 2020

Accepted: 09 January 2021

*Correspondence:

Dr. Dhakchinamoorthi Krishna Kumar,
E-mail: krishnakumarx@hotmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Antibiotic resistance is a major menace to public health and treatment of several infectious diseases, also associated with an economic burden to society. Pharmacoeconomic analysis of antibiotic usage and cost-minimization analysis provides better and low-cost drug selection for the patients.

Methods: The study was conducted as a cross-sectional, observational analysis of restricted antibiotics in the prescriptions (n= 191). Cost minimization analysis was conducted for the restricted antibiotics alone. The drug costs of prescribed brands were compared with the least cost brands, and the percentage cost difference was calculated and compared by student paired 't' test. P<0.05 considered statistical significance.

Results: The average age of the patients was found to be 58.1±18.3 (Mean±SD) years, and most of the restricted antibiotics were prescribed for the treatment of hospital-acquired infections 71.7%. Meropenem was prescribed highly 29.8% followed by imipenem (28.8%) and colistin (12%). The major reason for starting restricted antibiotics was found to be infectious diseases (27.7%). The cost-minimization analysis showed that the total unit cost for caspofungin (₹1,85,000 or \$2523.40) was found to be higher followed by meropenem (₹1,29,800) in the prescriptions. The mean cost of actually prescribed restricted antibiotics was found to be ₹68,338±61,332 (Mean±SD). The lowest mean cost of restricted antibiotics was found to be ₹32,223±31,082 (p<0.05).

Conclusions: Pharmacoeconomic cost-minimization analysis was a useful tool for clinical pharmacist in the selection of appropriate antibiotics and minimizing the burden of the cost of the drugs, it provides a better outcome in patients while using restricted antibiotics with infectious disease.

Keywords: Antimicrobial, Cost Minimization, Pharmacoeconomic, Restricted antibiotics

INTRODUCTION

Antibiotic resistance is considered as one of the worldwide health economic burdens. This can be mainly due to the inappropriate use of antibiotics.

The incidence of morbidity and mortality due to antibiotic resistance can be reduced by controlling the irrational use of antibiotics. In most hospitals, different types of guidelines have been implemented to improve the antibiotic prescribing practice which includes the

formation of antibiotic usage guidelines, restricted antibiotics prescribing documentation forms, computerized prescribing, and monitoring information systems for the selection of antimicrobials.¹ However, the antibiotic resistance pattern has been growing and challenging to treat infectious diseases.

The microorganisms may show resistance to both already marketed and also to a newer class of antibiotics. Wide resistant microorganisms such as bacteria, fungi, viruses, parasites can withstand against the action of antimicrobial drugs which makes standard treatment ineffective and increase the risks of infections, also these microorganisms are called as “superbugs”.²

Restricted antibiotics are those antibiotics that could contribute to acting against multi-resistance organisms. It is developed and targeted to ensure the effective use of antimicrobials and significantly reduces the resistance pattern among antimicrobial agents.³ Drug resistance is becoming a more serious condition and many infections may not be cured easily with existing protocol, leading to prolonged expensive treatment and increase the risk of death.³ Hence, monitoring antibiotic therapy and reducing the economic burden to the patient is difficult.

Pharmacoeconomics is a branch of the analytical method of health economics which compares the cost of pharmaceutical products and treatment strategies. The pharmacoeconomic method includes cost-minimization, cost-effectiveness, cost-benefit, and cost-utility analysis.⁴ Implementation of a program or methods and analysis of the cost of antimicrobial therapy showed the exact economic burden to the society as well as patients.^{4,5} In the present study, we have conducted a cost-minimization analysis (CMA) and calculated the total unit cost of restricted antibiotic usage in the patient's prescriptions. CMA compares the cost of available alternate antibiotic brands that have equivalence in therapeutic outcomes.

The clinical pharmacist can play an effective and important role in limiting the emergence of resistance and subsequent clinical consequence of antibiotic resistance by various pharmaceutical care activities involving and implementing strategies.^{1,6} Hence the basic information is a must to develop strategies. In the present study, the basic outline is preliminarily studied.

METHODS

The study was conducted as a cross-sectional, observational to analyze the usage pattern of restricted antibiotics and their cost-minimization analysis in Fortis hospital, Chennai. The study was approved by the institutional committee and conducted according to the declaration of Helsinki. The study was conducted for six months from January to June 2016. Patients' data were collected from medical records and patients prescribed any one or more restricted antibiotics were included for the study. Cost minimization analysis was conducted for

the restricted antibiotics alone. The cost of other drugs and other associated medical costs were not included in the analysis. The total cost for the actual prescribed drug along with low-cost drugs was compared for cost-minimization analysis.

The cost-minimization analysis was done by calculation as follows:

A. The total cost of individual restricted antibiotics prescribed (actual given brands cost) = [Unit cost of individual restricted antibiotics (actual given brands cost) × number of doses per day × number of days]

B. Total cost of individual restricted antibiotics prescribed (brand with least cost) = [Unit cost of individual restricted antibiotics (brand with least cost) × Number of doses per day × Number of days]

C. Total cost difference = Total cost of A - Total cost of B

D. Percentage of total cost difference = [(Total cost of B - Total cost of A) / Total cost of A] × 100

If more than one restricted antibiotic given calculated and added to total final costs in the same way of calculation of A and B for individual restricted antibiotics.

Statistical analysis

The statistical analysis was performed using Graph Pad prism 7.0. All data were expressed as percentage frequency and Mean±SD. The cost difference between the actual unit cost of prescribed restricted antibiotics with the lowest cost of available brands was compared by using a paired ‘t’ test. $p < 0.05$ was considered statistically significant.

RESULTS

In the present study, 191 prescriptions with restricted antibiotics were identified and included in the analysis. The average age of the patients was found to be 58.1±18.3 (Mean±SD) years. Many patients were in the age group of 70 years (25.7%) and 61-70 years (18.8%) followed by 51-60 years (19.9%). Among the total cases collected male: female percentage ratio was found to be 61:39%. The patients were grouped into four different categories (Type 1-Type 5). Based on their duration of hospital stay and requirement of the treatment among them, type 3 was reported high followed by type 2 (23%) (Figure 1). Meropenem was prescribed highly 29.8% followed by imipenem (28.8%) and colistin (12%). The maximum dose of meropenem was prescribed 2 gm (1.8%) in one prescription and a minimum dose was 500 mg (45.6%) observed in 26 (13.6%) prescriptions. The maximum dose of imipenem was 1 gm observed in 32.7% of prescriptions and a minimum dose of 500 mg observed in 52.7% of prescriptions. The major reason for

starting restricted antibiotics was found to be infectious diseases (27.7%) followed by sepsis (23.6%).

The restricted antibiotics were 71.7% prescribed for hospital-acquired infections and 28.3% for community-acquired infections. The restricted antibiotics were prescribed for various reasons (Figure 2) however, 52.9% of patients' culture reports were noted from the medical records.

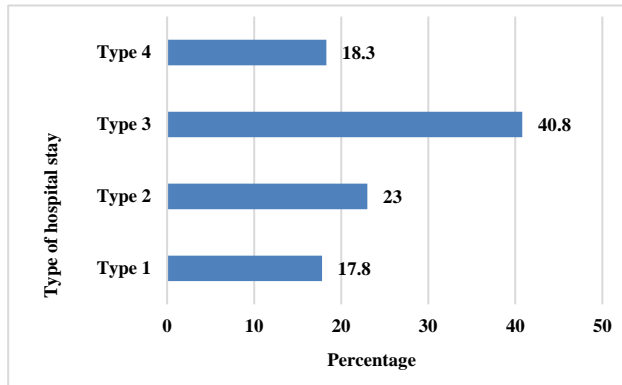


Figure 1: Patients categorized based on hospitalization (n=191).

TYPE 1: No prior contact with the health care system in the past 3 months.

TYPE 2: Contacted the healthcare system in the past 3 months or <1 week in the hospital or <48 hours in ICU without an invasive procedure.

TYPE 3: Long hospitalization (>1 week in the hospital or >48 hours in ICU) in the last 3 months and/or Type 2 with 1 or more invasive procedures/patient on dialysis.

TYPE 4: Type 3 with sepsis/ severe acute necrotizing pancreatitis/ tertiary peritonitis/ patient on TPN.

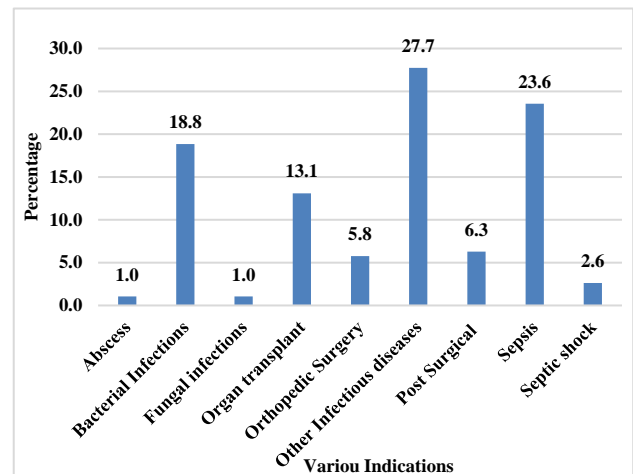


Figure 2: Percentage of restricted antibiotics usage for various conditions (n=191).

Table 1: Individual restricted antibiotics used and their unit and total cost (n=191).

Drug name	No of Prescription	Unit cost (total in ₹)	Total cost (total in ₹)
Caspofungin	13	185000	2750500
Amphotericin	3	33145	497175
Imipenem	55	86922.72	2151464.4
Colistin	23	68376.5	1036042
Meropenem	57	129800	2534050
Tigecycline	20	85863.93	1214698.92
Vancomycin	7	3640.4	23950
Linezolid	12	4560	72580
Micafungin	1	17733	248262

Table 2: Percentage cost difference and total actual unit cost of antibiotics with cheaper cost of available brands (n=191).

Drug name	Number of prescriptions	Actual unit cost (A) (₹)	Cheaper brand cost (B) (₹)	% cost difference
Caspofungin	13	185000	79920	-56.8
Amphotericin B	3	33145	1750	-94.7
Imipenem	55	86922.72	39765	-54.3
Colistin	23	68376.5	33365.28	-51.2
Meropenem	57	129800	82575	-36.4
Tigecycline	20	85863.93	28953.13	-66.3
Vancomycin	7	3640.4	2852.5	-21.6
Linezolid	12	4560	3096	-32.1
Micafungin	1	17733	17733	-

A vs B Compared by student paired 't' test, p<0.05.

The cost-minimization analysis was performed for restricted antibiotics, the unit cost for caspofungin (₹1,85,000 or \$2523.40) was found to be higher followed by meropenem (₹1,29,800) (Table 1). The total unit cost for all restricted antibiotics was found to be ₹. 6,15,041.55 and also the total cost for all the patients was found to be ₹.1,05,28,722.32 during the treatment period. In the total cost, caspofungin alone was found to be ₹.27, 50,500 followed by meropenem alone costs ₹.25, 34,050. The cost differences were analyzed between the actual unit cost of prescribed restricted antibiotics with less cost available brands of the same antibiotic and were compared (Table 2). We have observed a significant difference among the prescribed brands with low-cost brands ($p=0.0127$). The mean cost of actually prescribed restricted antibiotics was found to be ₹.68,338±61,332 (Mean±SD). The lowest mean cost of restricted antibiotics was found to be ₹.32,223±31,082. The percentage cost difference showed that 45.93% of the cost could be saved by selecting low-cost restricted antibiotics brands. Also, it was observed that Amphotericin B prescribed a 94.4% higher cost brand than the available least-cost brand, similarly tigecycline (66.3%).

DISCUSSION

The restricted antibiotic usage pattern in a corporate hospital and cost-minimization analysis was studied. In the present study, we have analyzed and one of the major reasons for the usage of restricted antibiotics was found to be prolonged hospitalization for infectious disease and hospital-acquired infections. The most widely used restricted antibiotic was found to be meropenem followed by imipenem because most of the organisms were sensitive to these antibiotics. A higher dose of meropenem followed by imipenem was used in a patient due to highly resistive organisms or complicated surgery conditions. This finding was similar in a previous study the usage of meropenem reported was higher.⁷

In recent days, the antibiotic usage pattern increased enormously with the various class of antibiotics for treating most infectious diseases. Some previous study reports revealed that the usage pattern in hospitalized patients was higher than the community patients.^{8,9} Also applying antibiotic stewardship practices are crucial to controlling the usage of high-end antibiotics.⁷ In the present study, most of the restricted antibiotics were prescribed for nosocomial infections (71.7%) and the finding was in agreement with the previous study.⁷ The prolonged hospital stay was the major reason for nosocomial infections and forces the physician to prescribe antibiotics to treat or prevent the infection.¹⁰ Further nosocomial infections lead to increased or prolonged the length of hospital stays also associated with increased medical care costs.^{11,12} Several studies demonstrated that the prescribing pattern of restricted antibiotics was increased in practice.^{13,14} The results revealed that the excessive use of certain antibiotics

remains a challenging problem. Frequently monitoring the usage of high-end antibiotics such as ceftazidime, imipenem, or meropenem and vancomycin were useful and promote rational drug use as well as to reduce drug resistance.¹⁵

Pharmacoeconomic analysis of antibiotics will provide a great insight into antibiotic selection and improving rational antibiotic usage pattern.⁹ Cost-effectiveness studies were conducted widely.¹⁶⁻¹⁸ Some studies have explained the benefits of cost-utility and cost-benefit as pharmacoeconomic analytical methods.¹⁹ However, the cost-minimization analysis provides a better selection of the low cost same antibiotic regimen for the underlying infectious conditions without affecting the treatment protocol.^{20,21} Also, the cost-minimization analysis required less personal and can be managed by a clinical pharmacist in his routine work. So, in the present study, CMA is done to establish the basic cost of restricted antibiotics in a tertiary care setting. The total unit cost of restricted antibiotics usage analysis in the present study population was found to be significantly higher (₹.1,15,46,025) when compared to non-restricted antibiotic usage. It was also observed that imipenem alone consumed a higher cost (₹.29,76,475). Hence, the resistance pattern of organisms forced the physician to prefer and prescribe a higher class of restricted antibiotics. However, in a previous study, it was observed that restricting the parenteral antibiotic usage leads to a significant decrease in expenditure burden on antibiotics by ₹ 1,45,911 (17.31%).²² However, in the present study, we have not conducted complete cost minimization and cost-utility analysis for all drugs prescribed and total treatment costs. We have observed that there was a significant preference in the total cost of actually prescribed restricted antibiotic drug and lower-cost brands available in the market. Also, the role of the clinical pharmacist was emphasized to add to bring down the irrational prescribing of restricted antibiotics. In previous studies were explained the role of clinical pharmacists in the hospital antibiotic stewardship and ensuring rational, safe, cost-effective treatment outcome among patients with infectious diseases.^{23,24}

CONCLUSION

The present study evaluated the usage pattern of restricted antibiotics and cost minimization analysis and there was a strong role of clinical pharmacist needed in the selection of appropriate antibiotics to ensure effective cost minimization of the antibiotic usage among the patients and also emphasized clinical pharmacist plays a significant role to ensure rational use of antibiotics. The appropriate selection of antibiotics and minimizing the burden of the cost of the drugs provide a better outcome in patients with infectious conditions.

ACKNOWLEDGEMENTS

Dr. Shankar, Clinical Pharmacologist, Dr. Akhila Raj, Dr. Ashik Aliyar, Dr. Shilpha, and Dr. Anishal Anna Paul,

Clinical Pharmacy students, C. L. Baid Metha College of Pharmacy and Nursing staff are gratefully acknowledged.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethics committee

REFERENCES

- Chandy SJ, Naik GS, Charles R, Jeyaseelan V, Naumova EN, Thomas K, et al. The impact of policy guidelines on hospital antibiotic use over a decade: a segmented time series analysis. *PLoS One*. 2014;9(3):e92206.
- The rise of superbugs. Dangerous infections that are resistant to antibiotics are spreading and growing stronger, with dire consequences. Medical experts say it's a mess of our own making--and the clock is ticking on when and how we must solve it. The first in a three-part series. *Consum Rep*. 2015;80(8):20-6.
- De Waele JJ, Akova M, Antonelli M, Canton R, Carlet J, De Backer D, et al. Antimicrobial resistance and antibiotic stewardship programs in the ICU: insistence and persistence in the fight against resistance. A position statement from ESICM/ESCMID/WAAAR round table on multi-drug resistance. *Intensive Care Med*. 2018;44(2):189-96.
- Lanbeck P, Ragnarson Tennvall G, Resman F. A cost analysis of introducing an infectious disease specialist-guided antimicrobial stewardship in an area with relatively low prevalence of antimicrobial resistance. *BMC Health Serv Res*. 2016;16:311.
- Sriram S, Aiswaria V, Cijo AE, Mohankumar T. Antibiotic sensitivity pattern and cost-effectiveness analysis of antibiotic therapy in an Indian tertiary care teaching hospital. *J Res Pharm Pract*. 2013;2(2):70-4.
- Wang J, Dong M, Lu Y, Zhao X, Li X, Wen A. Impact of pharmacist interventions on rational prophylactic antibiotic use and cost saving in elective cesarean section. *Int J Clin Pharmacol Ther*. 2015;53(8):605-15.
- Jayalakshmi J, Priyadarshini MS. Restricting high-end antibiotics usage - challenge accepted! *J Family Med Prim Care*. 2019;8(10):3292-6.
- Nair M, Tripathi S, Mazumdar S, Mahajan R, Harshana A, Pereira A, et al. "Without antibiotics, I cannot treat": A qualitative study of antibiotic use in Paschim Bardhaman district of West Bengal, India. *PLoS One*. 2019;14(6):e0219002.
- Mitchell ED, Czoski Murray C, Meads D, Minton J, Wright J, Twiddy M. Clinical and cost-effectiveness, safety and acceptability of community intravenous antibiotic service models: CIVAS systematic review. *BMJ Open*. 2017;7(4):e013560.
- Wolkewitz M, Schumacher M, Rucker G, Harbarth S, Beyersmann J. Estimands to quantify prolonged hospital stay associated with nosocomial infections. *BMC Med Res Methodol*. 2019;19(1):111.
- Kaye KS, Marchaim D, Chen TY, Baures T, Anderson DJ, Choi Y, et al. Effect of nosocomial bloodstream infections on mortality, length of stay, and hospital costs in older adults. *J Am Geriatr Soc*. 2014;62(2):306-11.
- Sheng WH, Chie WC, Chen YC, Hung CC, Wang JT, Chang SC. Impact of nosocomial infections on medical costs, hospital stay, and outcome in hospitalized patients. *J Formos Med Assoc*. 2005;104(5):318-26.
- Morales FE, Villa LA, Fernandez PB, Lopez MA, Mella S, Munoz M. Evolution of use of antibiotics of restricted prescription and trend of bacterial susceptibility in Concepcion Regional Hospital, Chile. *Rev Chilena Infectol*. 2012;29(5):492-8.
- Saridi M, Rekleiti M, Toska A, Kriebardis AG, Tsironi M, Syrigos K, et al. Appropriate utilization of restricted antibiotics in a general hospital of a prefecture area in Greece. *Curr Drug Saf*. 2014;9(3):212-9.
- Ayuthya SK, Matangkasombut OP, Sirinavin S, Malathum K, Sathapatayavongs B. Utilization of restricted antibiotics in a university hospital in Thailand. *Southeast Asian J Trop Med Public Health*. 2003;34(1):179-86.
- Oppong R, Kodabuckus S. Cost-effectiveness of outpatient parenteral antibiotic therapy for children with cellulitis. *Lancet Infect Dis*. 2019;19(10):1041-2.
- Friedlander AH, Chang TI, Aghazadehsanai N, Graves LL. Cost-effectiveness of antibiotic prophylaxis. *J Am Dent Assoc*. 2016;147(4):229-30.
- Holmes EAF, Harris SD, Hughes A, Craine N, Hughes DA. Cost-Effectiveness Analysis of the Use of Point-of-Care C-Reactive Protein Testing to Reduce Antibiotic Prescribing in Primary Care. *Antibiotics (Basel)*. 2018;7(4).
- Grotle M, Braten LC, Brox JI, Espeland A, Zolic-Karlsson Z, Munk Killingmo R, et al. Cost-utility analysis of antibiotic treatment in patients with chronic low back pain and Modic changes: results from a randomised, placebo-controlled trial in Norway (the AIM study). *BMJ Open*. 2020;10(6):e035461.
- Dik JW, Hendrix R, Friedrich AW, Luttjeboer J, Panday PN, Wilting KR, et al. Cost-minimization model of a multidisciplinary antibiotic stewardship team based on a successful implementation on a urology ward of an academic hospital. *PLoS One*. 2015;10(5):e0126106.
- Lee KK, Wan MH, Fan BS, Chau MW, Lee VW. A cost-minimization analysis comparing different antibiotic regimens used in treating all-cause bacterial pneumonia in Hong Kong. *J Med Econ*. 2009;12(1):46-55.
- Tiwari SA, Ghongane BB, Daswani BR, Dabhade SS. Restricted Parenteral Antibiotics Usage Policy

in a Tertiary Care Teaching Hospital in India. *J Clin Diagn Res.* 2017;11(5):FC06-9.

23. Almulhim AS, Aldayyen A, Yenina K, Chiappini A, Khan TM. Optimization of antibiotic selection in the emergency department for urine culture follow ups, a retrospective pre-post intervention study: clinical pharmacist efforts. *J Pharm Policy Pract.* 2019; 12:8.
24. Alvaro-Alonso EA, Aldeyab M, Ashfield L, Gilmore F, Perez-Encinas M. "International Centres

of Excellence in Hospital Pharmacy"; a SEFH new initiative; the role of the clinical pharmacist in the hospital antibiotic stewardship in Northern Ireland. *Farm Hosp.* 2016;40(4):233-6.

Cite this article as: Kumar DK, Swapna M, Kanmani S, Varsha V, Vidya NV. Evaluation of restricted antibiotic utilization and cost-minimization analysis (CMA) in a tertiary care hospital in India. *Int J Sci Rep* 2021;7(2):116-21.