

## THE PHARMA INNOVATION

# Antibiotic Prescription and Cost Patterns In An Intensive Care Unit: A Review of Literature

Amit Singh Gangwar<sup>1\*</sup>, Neeraj Kumar<sup>1</sup>, Preeti Kothiyal<sup>1</sup>

1. Department of Clinical Pharmacy, Division of Pharmaceutical Sciences, Shri Guru Ram Rai Institute of Technology and Science, Patel Nagar, Dehradun, Uttarakhand, India

Patients admitted to the ICU are seriously ill and often suffer from chronic critical illnesses. Antibiotics are the most frequently prescribed drugs among hospitalized patients especially in intensive care and surgical department. Antibiotic to resistance of common hospital-acquired bacteria is a worldwide problem. It can lead to increased morbidity, mortality, length of hospital stay, and healthcare expenditures. An ICU of a developing country where health costs are borne by the patients and to some extent the hospitals, it is causing a huge economic burden. Institutions elsewhere in the world have enhanced patient care through therapeutic optimization of the use of antimicrobial agents through the use of antibiotic restriction policies implemented widely throughout the hospital. Knowledge of an ICUs most common bacterial isolates and their antibiotic susceptibility patterns facilitates effective empirical antibiotic therapy and supports decisions to restrict or reduce the clinical availability of certain antibiotics.

*Keyword:* Admission, Antibiotic Usage, Intensive Care Unit, Prescriptions

### INTRODUCTION:

#### Antibiotics Use in ICU for Prescribing Practices

Patients admitted to the ICU are seriously ill and often suffer from chronic critical illnesses. Antibiotics are the most frequently prescribed drugs among hospitalized patients especially in intensive care and surgical department [1]. Antibiotic to resistance of common hospital-acquired bacteria is a worldwide problem.

Corresponding Author's Contact information:  
Amit Singh Gangwar \*  
Department of Pharmaceutical Sciences, S.G.R.R.I.T.S.,  
Patel Nagar, Dehradun, India.  
E-mail: amitgangwar12@gmail.com

It can lead to increased morbidity, mortality, length of hospital stay, and healthcare expenditures [2].

Drug use pattern study from an ICU in Northern India, the average age of patient studied was 49 years with an average LOS of 5.75 days, total number of patient discharged 60.50% and expired 39.50% [3]. Similarly, drug use patterns study from an ICU in Iran, the average age of patients studied was 50 years with an average LOS of 6 days [4] and other data reported that the average duration of patient stay in the ICU was 7 days [5]. The average number of drugs per prescription is an important index of a prescription audit. It is recommended that the number of drugs per

prescription should be kept as low as possible to minimize the risk of drug interactions, development of bacterial resistance, and hospital costs [6].

Drug use pattern study from an ICU in Northern India, 200 patients received 1246 drugs and 418 antibiotics during their stay in the hospital, the average number of drugs and antibiotics prescribed per patient were 6.23 and 2.09, antibiotics constituted 33.54% of the total drug prescribed. There were 14 patients in total who received more than 10 drugs and 51 patients who received 3 or more than 3 antibiotics during their stay in the ICU [3] and other data reported in literature, ranging from 5.1 to 12, according to the type of patient population and the geographical location studied [7,8].

Drug use pattern study from an ICU in Northern India, a number of patients were prescribed an antibiotic at admission 95% [3]. Other data reported that the nearly 62% patients in a tertiary care ICU in northern India received antibiotics [9], while 64% of ICU patients received empiric antibiotics [10]. A survey on antibiotic prescribing patterns in ICUs of Australia and New Zealand revealed that a total of 656 antibiotics were "empirically" prescribed by 84 intensivists during the 4-month study period and the main areas for noncompliance with guidelines were provision for broader cover for resistant infections [11]. Data from other countries report 60%-75% rates of antibiotic prescription in the ICU [12,13] and studies from Europe report an average antibiotic use of 58%-61% [5,14]. In a relatively older study on antibiotic usage patterns, of the 220 patients receiving antibiotics for an infection in a Danish ICU, 87% were treated on day 1, but only 34% on day 11 [15].

Drug use pattern study from an ICU in Northern India, most patients (70%) received 2 or less antibiotics [3] and 60% of the patients studied in a Caribbean ICU received two antimicrobials [16]. Data from the western ICUs indicates that fewer antimicrobials are prescribed in western ICUs. A study in a Danish university hospital

ICU reported that the majority of their patients were on one antibiotic [14], whereas in a German surgical ICU, 36.7% of cases were treated with only one antibiotic agent, 14.1% were given a combination of 2, and 7.2% were given a combination of  $\geq 3$  antibiotic agents [17].

The most commonly prescribed antibiotics in ICU reported that penicillin, 1<sup>st</sup> generation cephalosporins, aminoglycosides, nitroimidazoles, fluoroquinolones, tobramycin, ofloxacin, cefuroxime, Amikacin, Cefoperazone+Sulbactam, Amoxicillin+ Clavulanic and Ceftriaxone etc [18,19,20,21].

### Concept For Defined Daily Dose

The DDD is the assumed average maintenance dose per day for a drug used for its main indication

in adults. DDD can be used as a tool to analyze drug utilization with the ultimate goal of improving drug use. DDD are advantageous for comparing the use of drug in hospitals or regions. This comparison will provide valuable information when establishing appropriate usage level of drugs. The DDD is nearly always a compromise dose, not the actual dose used. The DDD may even be a dose that is seldom prescribed, because it is an average of two or more commonly used dose sizes [22].

### Methods Of Defined Daily Dose

There are several different methods for utilizing DDD to describe drug consumption.

#### 1) DDDs per 1000 inhabitants per day

It may provide a rough estimate of proportion of the study population treated daily with a particular drug. This estimate is most useful for chronically used drug. It is most frequently used method for DDD [22].

#### 2) DDDs per 100 bed-days

The DDDs per 100 bed-days may be applied when drug use by inpatients is considered. The definition of a bed-day may differ between hospitals or countries, and bed- days should be

adjusted for occupancy rate. This unit is quite useful for benchmarking in hospitals [22].

$$\text{DDD}/100 \text{ bed-days} = \frac{\text{No. of units administered in a given period (mg)} \times 100}{\text{DDD (mg)} \times \text{no. of days in the period} \times \text{no. of beds} \times \text{occupancy index}} \quad [7]$$

### 3) DDDs per inhabitant per year

The DDDs per inhabitant per year may give an estimate of the average number of days for which each inhabitant is treated annually [22].

#### Different Study For Use Of Antibiotics In ICU By Defined Daily Dose

Drug use pattern study from an ICU in Northern India, the DDD/100 bed-days for the 5 most frequently prescribed antibiotics were found to be 18.48 (3<sup>rd</sup> generation cephalosporins), 14.65 (metronidazole), 15.97 (levofloxacin), 16.47 (meropenem), and 13.42 (ceftriaxone) [3] and other data reported that in India, the most frequently prescribed antibiotic was metronidazole followed by cefotaxime, amoxicillin/clavulanic acid, cefipime, and ciprofloxacin [9]. The utilization of penicillins, fluoroquinolones, 2nd-generation cephalosporins and 3rd-generation cephalosporins were 55.1, 5.34, 0.82, and 13.74 DDD/100 bed-days, respectively [7]. The use of antibiotics in a Brazilian hospital had increased from 83.8 DDDs/100 bed-days in 1990 to 124.6 DDDs/100 bed-days in 1996 [23]. The introduction of a hospital antibiotic policy helped to reduce antibiotic utilization at a university hospital from 45.9 DDDs/100 bed-days to 32.9 DDDs/100 bed-days [24]. Total antibiotic consumption was markedly reduced from 162.9 to 101.3 defined daily dose (DDD) per 100 patients, and per day (DDD per 100 patient-days) [25].

#### Different Study For Costs Of Antibiotic In ICU

Drug use can be expressed in terms of costs (eg: national currency). Cost figures are suitable for an overall analysis of expenditure on drugs.

International comparisons based on cost parameters can be misleading and have limited value in the evaluation of the drug use [22]. An ICU of a developing country where health costs are borne by the patients and to some extent the hospitals, it is causing a huge economic burden [26].

Drug use pattern study from an ICU in Northern India, the cost analysis of the antibiotics and the total drugs prescribed at admission revealed that patients were prescribed drugs and antibiotics worth nearly Rs 2725 per patient and Rs 1995 per patient respectively, antibiotic costs accounted for 73.2% of the total drug expenditure and meropenem was the most expensive drug ordered (accounting for 34.7% of the total antibiotic costs) [3], while the patients spent about Rs 19,725 on total drug costs and antibiotics contributed to 51.3% of the total drug expenditure [9]. Nepal report an average expenditure of Rs 1958.53 ± 1267.8 on the drugs prescribed in ICU [7]. Data from the western literature report ICU drug costs per patient-day ranging from \$208 to \$312 [27]. The costs incurred due to antibiotic usage in bloodstream infections in 310 patients in an ICU in Belgium, the mean overall daily antimicrobial cost was €114.25, with higher costs in patients with nosocomial infections [28]. In a Turkish university hospital, the mean daily antibiotic cost was \$89.64, with higher costs for patients with nosocomial infections and meropenem was the most expensive drug for treatment in this group [29].

#### Impact Of Antibiotic Restriction On Antibiotics Usage In ICU

Institutions elsewhere in the world have enhanced patient care through therapeutic optimization of the use of antimicrobial agents through the use of antibiotic restriction policies implemented widely throughout the hospitals [30]. Knowledge of an ICUs most common bacterial isolates and their antibiotic susceptibility patterns facilitates effective empirical antibiotic therapy and supports decisions to restrict or reduce the clinical availability of certain antibiotics [31].

The implementation of rational antibiotic policies have had a significant positive economic benefit and improved quality of care delivered to patients [32]. The use of a computerized decision support tool, which reduced their total antibiotic utilization by 10.55% and increased the number of switches to narrow spectrum antibiotics [33]. Implementation of local antibiotic management programs, infectious disease specialist consultation, and restricted authorization to prescribe antibiotics have all been reported to result in marked reductions in antibiotic consumption [25]. A developing country, found that creation of a restriction program using an infectious disease specialist helped reduce the antibiotic prescriptions of broad spectrum antibiotics by 34% [34]. The use of diagnosis-related groups (DRG)-based health care systems have also been suggested in order to reduce costs of antibiotic therapy. Here, it is possible to identify subsets of infections and the patient records that have a potentially negative DRG-result, that is, the costs are higher than the reimbursement. This can help to find out if a different therapeutic approach, for example, by different choices in initial (empirical) antibiotic treatment may cause other outcomes leading to a better balance of clinical and economical outcomes in patients with severe infections [35].

### Conclusion

Antibiotics are commonly prescribed to most ICU patients at time of admission. Antibiotics continue to be widely prescribed in critically ill patients and form a significant proportion of the total drugs consumed in the ICU. The elderly and sicker patients are prescribed more antibiotics in ICU, especially antibiotics that are more expensive. The high utilization rates and costs of antibiotics prescribed at admission in the ICU are a matter of great concern and need to be improved by the use of guidelines, surveillance and antibiotic restriction policies of health care.

### REFERENCE:

1. Krivoy N, El-Ahal WA, Bar-Lavie Y, Haddad S. Antibiotic prescription and cost patterns in a general intensive care unit. *Pharmacy Practice* 2007; 5(2):67-73.
2. Bassetti M, Di Biagio A, Rebesco B, Amalfitano ME, Topal J, Bassetti D. The effect of formulary restriction in the use of antibiotics in an Italian hospital. *Eur J Clin Pharmacol* 2001; 57:529-34.
3. Williams A, Mathai AS, Phillips AS. Antibiotic prescription patterns at admission into a tertiary level intensive care unit in Northern India. *J Pharm Bioall Sci* 2011; 3:531-6.
4. Tavallaee M, Fahimi F, Kiani S. Drug-use patterns in an intensive care unit of a hospital in Iran: An observational prospective study. *Int J Pharm Pract* 2010; 18:370-6.
5. Bergmans DCJJ, Bontena MJM, Gaillard CA, Van Tiel FH, Van der Geesta S, De Leeuwa PW et al. Indications for antibiotic use in ICU patients: A one-year prospective surveillance. *J Antimicrob Chemother* 1997; 39:527-35.
6. Stratton CW 4<sup>th</sup>, Ratner H, Johnston PE, Schaffner W. Focused microbiological surveillance by specific hospital unit: Practical application and clinical utility. *Clin Ther* 1993; 15(Suppl A):12-20.
7. Shankar PR, Partha P, Dubey AK, Mishra P, Deshpande VY. Intensive care unit drug utilization in a teaching hospital in Nepal. *Kathmandu Univ Med J (KUMJ)* 2005; 3:130-7.
8. Smythe MA, Melendy S, Jahns B, Dmuchowski C. An exploratory analysis of medication utilization in a medical intensive care unit. *Crit Care Med* 1993; 21:1319-23.
9. Biswal S, Mishra P, Malhotra S, Puri GD, Pandhi P. Drug Utilization Pattern in the intensive care unit of a tertiary care hospital. *J Clin Pharmacol* 2006; 46:945-51.
10. Shrikala B, Kranthi K, Nafisa. A prospective study on a evaluation of antibiotic prescription practice in an intensive care unit of a tertiary care hospital. *J Clin Diag Res* 2010; 4:3387-91.
11. Dulhunty JM, Webb SA, Paterson DL, Bellomo R, Myburgh J, Roberts JA et al. A survey of antibiotic prescribing practices in Australian and New Zealand intensive care units. *Crit Care Resusc* 2010; 12:162-70.
12. Erbay A, Bodur H, Akinci E, Colpan A. Evaluation of antibiotic use in intensive care units of a tertiary care hospital in Turkey. *J Hosp Infect* 2005; 59:53-61.
13. Hanssens Y, Ismaeil BB, Kamha AA, Elshafie SS, Adheir FS, Saleh TM et al. Antibiotic prescription

- pattern in a medical intensive care unit in Qatar. *Saudi Med J* 2005; 26:1269-76.
14. Hartmann B, Junger A, Brammen D, Klasen J, Quinzio L. Review of antibiotic drug use in a surgical ICU: management with a patient data management system for additional outcome analysis in patients staying more than 24 hours. *Clin Ther* 2004; 26:915-24.
  15. Roder BL, Nielsen SL, Magnussen P, Engquist A, Frimodt-Moller N. Antibiotic usage in an intensive care unit in a Danish university hospital. *J Antimicrob Chemother* 1993; 32:633-42.
  16. Hariharan S, Pillai G, McIntosh D, Bhanji Z, Culmer L, Harper-McIntosh K. Prescribing patterns and utilization of antimicrobial drugs in a tertiary care teaching hospital of a Caribbean developing country. *Fundam Clin Pharmacol* 2009; 23:609-15.
  17. Meyer E, Jonas D, Schwab F, Rueden H, Gastmeier P, Daschner FD. Design of a surveillance system of antibiotic use and bacterial resistance in German intensive care units. *Infection* 2003; 31(4):208-15.
  18. Farooqi R, Afridi M, Farooqi J. Use of antibiotics in hospitalized adult patients: An experience from NWFP. *Rawal Medical Journal* 2005; 30:16-18.
  19. Fonseca, Lucieni. Audit of antibiotic use in Brazilian University Hospital. *Braz J Infect Dis* 2004; 8(4):272-280.
  20. Adiga MNS, Alwar MC, Pai MRS, Adiga US. Pattern of antimicrobial agents use in hospital deliveries: A prospective comparative study. *Online J Health Allied Scs.* 2009; 8(4):10.
  21. Patil P.H, Kuchake V.G, Kumar Ajay, Dighore Pitambar, Surana S.J. Evaluation of drug utilization especially antimicrobial agent pattern in tertiary care unit hospital. *International Journal of Community Pharmacy* 2009; 2(3):13-23.
  22. WHO Collaborating Centre for Drug Statistics Methodology. ATC index with DDDs. Oslo: WHO Collaborating Centre for Drug Statistics Methodology; 2002.
  23. Castro MS, Pilger D, Ferreira MB, Kopittke L. Trends in antimicrobial utilization in a university hospital, 1990–96. *Rev Saude Publica* 2002; 36:553-558.
  24. Vlahovic-Palcevski V, Morovic M, Palcevski G. Antibiotic utilization at the university hospital after introducing an antibiotic policy. *Eur J Clin Pharmacol* 2000; 56:97-101.
  25. Peto Z, Benko R, Matuz M, Csullog E, Molnar A, Hajdu E. Results of a local antibiotic management program on antibiotic use in a tertiary intensive care unit in Hungary. *Infection* 2008; 36(6):560-4.
  26. Keuleyan E, Gould M. Key issues in developing antibiotic policies: From an institutional level to Europe-wide. European Study Group on Antibiotic Policy (ESGAP), Subgroup III. *Clin Microbiol Infect* 2001; 7(Suppl 6):16-21.
  27. Weber RJ, Kane SL, Oriolo VA, Saul M, Skledar SJ, Dasta JF. Impact of intensive care drug costs: A description analysis, with recommendations for optimizing ICU pharmacotherapy. *Crit Care Med* 2003; 31:17-24.
  28. Vandijck DM, Depaemelaere M, Labeau SO, Depuydt PO, Annemans L, Buyle FM et al. Links Daily cost of antimicrobial therapy in patients with Intensive Care Unit-acquired, laboratory-confirmed bloodstream infection. *Int J Antimicrob Agents* 2008; 31:161-5.
  29. Inan D, Saba R, Gunseren F, Ongut G, Turhan O, Yalcin AN et al. Daily antibiotic cost of nosocomial infections in a Turkish university hospital. *BMC Infect Dis* 2005; 5:5.
  30. Sirinavin S, Suvanakoot P, Sathapatayavongs B, Malatham K. Effect of antibiotic order form guiding rational use of expensive drugs on cost containment. *Southeast Asian J Trop Med Public Health* 1998; 29:636-42.
  31. Kollef MH. Optimizing antibiotic therapy in the intensive care unit setting. *Crit Care* 2001; 5:189–195.
  32. Blanc P, Von Elm BE, Geissler A, Granier I, Boussuges A, Durand Gassel J. Economic impact of a rational use of antibiotics in intensive care. *Intensive Care Med* 1999; 25:1407-12.
  33. Thursky KA, Buising KL, Bak N, Macgregor L, Street AC, Macintyre CR. Reduction of broad-spectrum antibiotic use with computerized decision support in an intensive care unit. *Int J Qual Health Care* 2006; 18:224-31.
  34. Siddiqui S, Hussein K, Manasia R, Samad A, Salahuddin N, Zafar A et al. Impact of antibiotic restriction on broad spectrum antibiotic usage in the ICU of a developing country. *J Pak Med Assoc* 2007; 57:484-7.
  35. Wilke MH, Grube R. Pharmaco-economic evaluation of antibiotic therapy strategies in DRG- based healthcare system- a new approach. *Eur J Med Res* 2010; 15:564-70.