ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Antibiotic Use Density in Medicine ICU in a Tertiary Care Rural Hospital of Central India

Kavar KS*, Jha RK, Gaikwad NR, Jarande SS, Ranpura AM.

Department of Pharmacology, Jawaharlal Nehru Medical College, Sawangi (Meghe), Wardha, Maharashtra, India.

ABSTRACT

The objective of the study is to evaluate the pattern of usage of antibiotics and to find out Antibiotic Use Density in Medicine ICU. Case Sheets of patients admitted to Medicine ICU of tertiary care rural hospital during 1st October 2010 to 31st March 2011 were obtained from the Medical Record Department, studied and analysed critically. The drugs were classified according to Anatomical Therapeutic Chemical/Defined Daily Dose (ATC/DDD) system and antibiotic use density (AD) was calculated. A total of 610 patients were admitted and occupancy index was 74%. E.coli, H.influenzae, S.aureus and K. pneumonia were common organisms isolated and were found to be resistant to some of the commonly used antibiotics. Antibiotics were prescribed in 56.7% of patients. Total AD was found to be 287.9 DDD/100 patient-days (DDD_{100}). Third generation cephalosporin was the most frequently prescribed drug class (85.6 DDD_{100}) followed by fluoroquinolones (47.9 DDD_{100}) and penicillins + beta-lactamase inhibitors (46.1 DDD_{100}). The high percentage of inappropriate use of antimicrobials raises concerns about the development and spread of drug resistance. Regular auditing of antimicrobial prescriptions and prescribers' education to improve prescribing patterns to prevent their inappropriate use and unnecessary cost to the patients are required.

Key Words: Antibiotic Use Density, Defined Daily Dose, Intensive Care Unit, Antibiotic resistance

Corresponding author
Email: drkskavar@gmail.com

ISSN: 0975-8585

INTRODUCTION

The discovery of antibiotic agent represents one of the most important milestones in the advancement of medical sciences, as the use of antibiotics have successfully treated and cured many infectious diseases which were responsible for widespread morbidity and mortality in developing world.

Although antibiotics represent one of the most frequently prescribed classes of drugs among all hospitalized patients, total antibiotic consumption is much higher in the ICU than in general hospital wards. [1, 2]

Several authors [3-5] have reported concern about the continuous ubiquitous, indiscriminate and excessive use of antimicrobial agents that promote the emergence of antibiotic-resistant organisms. Patients with critical illnesses in the ICU setting are at risk of acquiring serious nosocomial infections which may lead to escalation in medical expenses, morbidity and mortality. [6]

Despite numerous guidelines from governmental and professional groups, there is broad evidence that antibiotics are prescribed inappropriately in up to 50% of cases. [7]

Various strategies have been proposed with the aim of moderating the emergence of bacterial resistance in the hospital environment. [8] However, the success of such measures depends largely on the availability of information regarding the form in which antibiotics are administered and salient factors relating to their excessive or inadequate use, particularly in ICUs.

Keeping in mind all these factors periodic surveillance and evaluation of antibiotic drug utilization in the ICU over a period of time are important.

World Health Organization (WHO) strongly recommends the Anatomical Therapeutic Chemical (ATC) classification system and the Defined Daily Dose (DDD) as a measurement unit for drug utilization studies [9]. In this system, drugs are categorized into various groups according to the organ or system upon which they act and according to their pharmacological and therapeutic properties. Defined daily dose (DDD) represents the average adult daily maintenance dose of a specific drug applied according to its primary indication. Antibiotic use Density is expressed as Defined Daily doses/ 100 patient- days.

To the best of our knowledge, no published studies have evaluated the Antibiotic Use Density (AD) in medicine ICU in India using Anatomical Therapeutic Chemical/Defined Daily Dose (ATC/DDD) system.

ISSN: 0975-8585

The objective of this study is to evaluate the pattern of usage of antibiotics and to find out antibiotic use Density in Medicine ICU.

MATERIALS AND METHODS

A retrospective study was carried out from the Case Sheets of patients admitted in Medicine ICU during the time period from 1st October 2010 to 31st March 2011. The hospital is 1000 bed tertiary level rural hospital of central India with a 13 bed medicine ICU that receives patients from within the hospital as well as ones referred from outside.

Analysis of record forms from the Medical Record Department was carried out. The age and sex distribution of the patients were noted. The duration of hospitalization in the ICU and the residential address of the patients were recorded. For calculating the duration of hospitalization, the day of admission was included but the day of discharge was excluded. The diagnosis/diagnoses recorded in the discharge summary were noted. Occupancy index was calculated using the following formula

$$\text{Occupancy Index} = \frac{\text{Total patient days x 100}}{\text{Number of days x bed strength}}$$

The patient outcome following the period of hospitalization in the ICU was studied. Patients could have been transferred to the ward, could have been discharged, referred for further management or may have left against medical advice. Some patients may have been discharged at request or may have died during the period of hospitalization.

The drugs prescribed during the period of hospitalization in the ICU were noted. The number of patients who had received an antibiotic during the period of stay in the ICU was determined. Number of drugs prescribed by the parenteral route was calculated. The drugs were classified according to the Anatomical Therapeutic Chemical (ATC) classification system (ATC/DDD version 2010).

The specimens sent for culture and sensitivity testing was enumerated. The organisms isolated and their antibiotic sensitivity patterns were recorded.

Antibiotic drug utilization was expressed in two ways - the total number of DDDs/100 patient-days and the percentage of patients receiving any particular antibiotics.

The Antibiotic Use Density (AD) was expressed as DDD/100 patient-days (DDD_{100}) and it was calculated using the following formula

$$\text{AD} = \frac{\text{Drug consumption in the study period (Gm) x 100}}{\text{DDD (Gm) x study period x bed strength x avg. occupancy}}$$

Drug consumption was calculated as sum of amount (gm) of that antibiotics used in each patient during the study period. In the denominator, DDD of specific drug was obtained

ISSN: 0975-8585

from the WHO website which is multiply by total number of days of study period (182 days in our study), bed strength of medicine ICU (13) and average occupancy in medicine ICU (0.74) during the study period.

RESULTS

A total of 610 individuals were admitted during the study period. Three hundred ninety four were male with male /female ratio of 1.8:1. Figure 1 show the age and gender distribution of the patients. The average age of patients admitted in medicine ICU was found to be 43.84 ± 17.9 years. 12.6% patients had a length of stay (LOS) more than 7 days. Average length of stay of patients was 5.14 days.

Figure 1: Age and sex distribution of patients admitted in medicine ICU

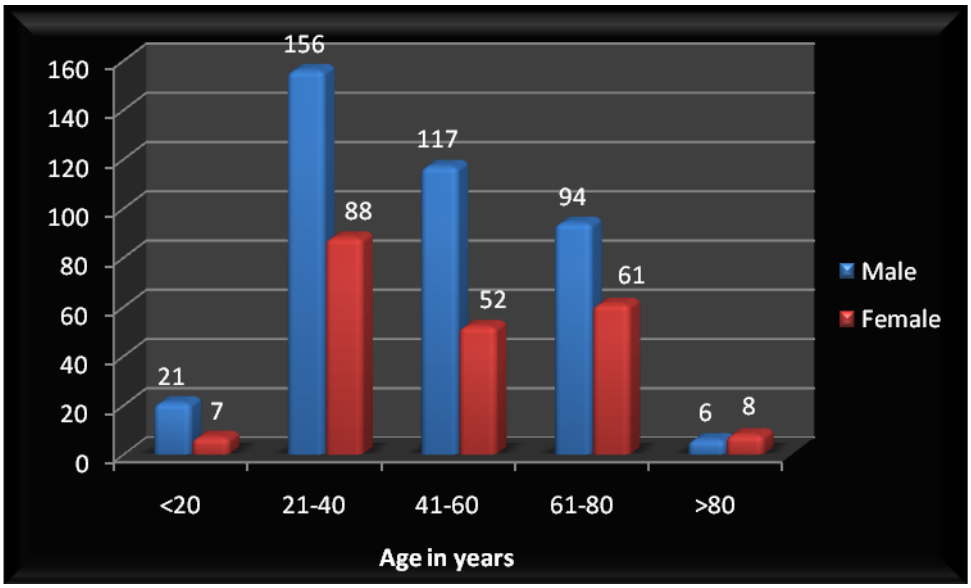


Table 1: Co-morbid conditions of patients on admission in Medicine ICU (n=610)

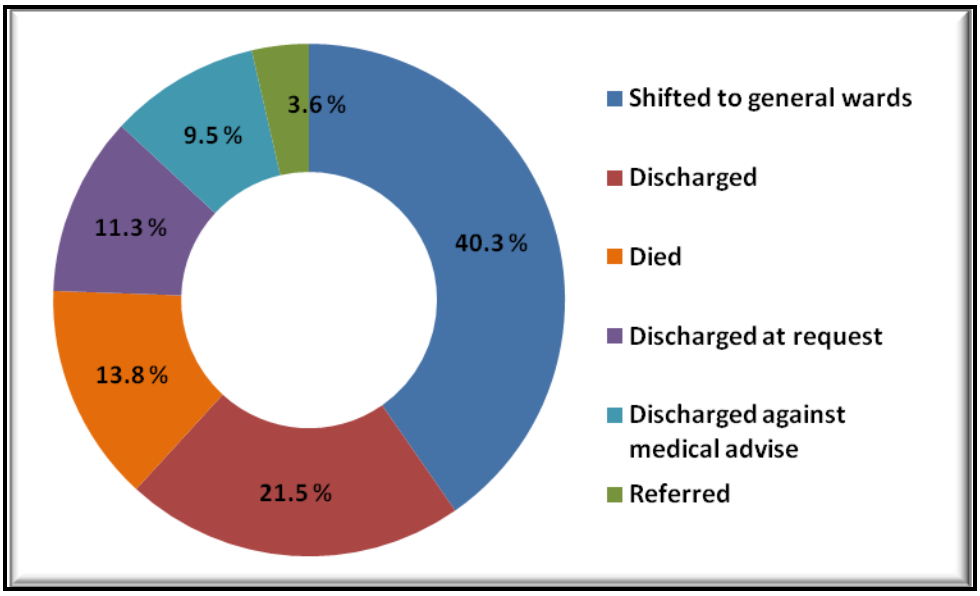
S No.	Co-morbid conditions	No. of patients (%)
1	Respiratory diseases	316 (51.8)
2	Diabetes mellitus	150 (24.6)
3	Cardiovascular diseases	217 (35.6)
4	Neurological disorders	121 (19.8)
5	Malignancy	31 (5.1)
6	Chronic renal failure	87 (14.2)
7	Chronic liver disease	165 (27.1)
8	Chronic alcoholic	189 (30.9)
9	Chronic smoker	157 (25.7)
10	Immunosuppressed	24 (3.93)
11	On steroids	108 (17.7)

ISSN: 0975-8585

Table No.1 enumerates co-morbid conditions found in patients during study period. Respiratory diseases (51.8%), cardiovascular diseases (35.6%) and chronic liver diseases (27.1%) were more common. 30.9 % of patients were chronic alcoholics while 25.7% were chronic smokers.

Total of 3269 drugs were prescribed during the period of stay in ICU. Mean ± SD number of drugs prescribed was 6.3 ± 2.1. Parenteral drugs accounted for 64.7% of the total drugs prescribed.

Figure 2: Patient outcomes following the period of hospitalization in medicine ICU



The patient's outcomes following the period of stay in the ICU are shown in Figure 2. 236 patients were shifted to the general wards while 19.8% patients were discharge from ICU after cure. Mortality rate in ICU found to be 13.7 % during the study period.

A total of 184 specimens were sent for culture and sensitivity testing. The specimens were collected from 153 patients. Blood (66 specimens), sputum (63 specimens) and urine (49 specimens) were the most common specimens collected.

ISSN: 0975-8585

Table2: Microbial sensitivity patterns of common microorganisms isolated from the medicine ICU

Antibiotic	Organism isolated % sensitivity (No. of cultures sensitive / No. tested)				
	E. coli	S. aureus	H. influenza	K. Pneumoniae	P. aeruginosa
Ampicillin	75 (3/4)	25 (1/4)	80 (4/5)	16.6 (1/6)	20 (1/5)
Amikacin	80 (4/5)	0 (0/3)	50 (1/2)	83.3 (5/6)	66.6 (2/3)
Ceftriaxone	100 (6/6)	75 (3/4)	83.3 (5/6)	0 (0/3)	80 (4/5)
Amoxicillin	0 (0/5)	0 (0/1)	75 (3/4)	0 (0/2)	0 (0/1)
Norfloxacin	66.6 (2/3)	100 (3/3)	NA	0 (0/3)	100 (2/2)
Cefotaxime	100 (5/5)	100 (4/4)	100 (4/4)	20 (1/5)	100 (3/3)
Gentamycin	85.7 (6/7)	NA	NA	100 (2/2)	66.6 (4/6)
Piperacillin	100 (2/2)	100 (1/1)	NA	66.6 (2/3)	100 (2/2)

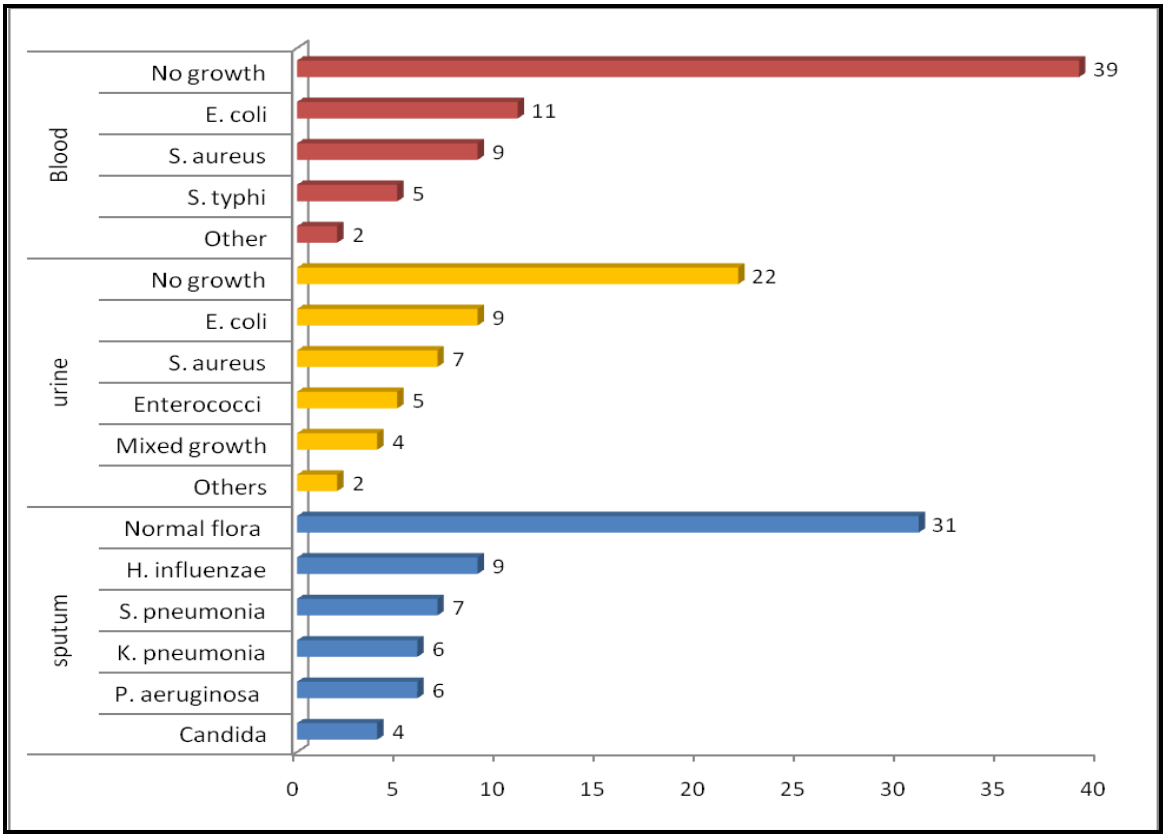
E.coli, H.influenzae, S.aureus, K. pneumoniae and P.aeruginosa were the most common organisms isolated on culture and sensitivity testing. The commonest organisms isolated from blood, sputum and urine are shown in figure no. 3. The antimicrobial sensitivity patterns of the common microorganisms are shown in Table 3.

Table 3: Frequently used antibiotic agent in medicine ICU of rural hospital.

S No.	Drug	Group	Number of patients	Percentage
1	Ceftriaxone	3rd Gen. cephalosporins	146	23.93
2	Piperacillin +Tazobactam	Combination of penicillins including beta lactamase inhibitors	103	16.89
3	Metronidazole	Imidazole derivatives	101	16.56
4	Amoxicillin + Clavulanic acid	Combination of penicillins including beta lactamase inhibitors	94	15.41
5	Cefuroxime	2nd Gen. cephalosporins	71	11.64
6	Cefexime	3rd Gen. cephalosporins	63	10.33
7	Ampicillin	Penicillins with extended spectrum	46	07.54
8	Ciprofloxacin	Fluoroquinolones	39	06.39
9	Cefepime	4th Gen. cephalosporins	35	05.74
10	Amikacin	Other aminoglycocide	32	05.25

ISSN: 0975-8585

Figure No.3: Organisms isolated from blood, urine and sputum specimens in Medicine ICU



Antibiotics were prescribed in 346 patients (56.7%) out of total patient admitted in ICU during the study period.

The route of administration of antimicrobials was intravenous for 36%, oral for 55% and by other routes for 9% of the total antibiotic agents prescribed.

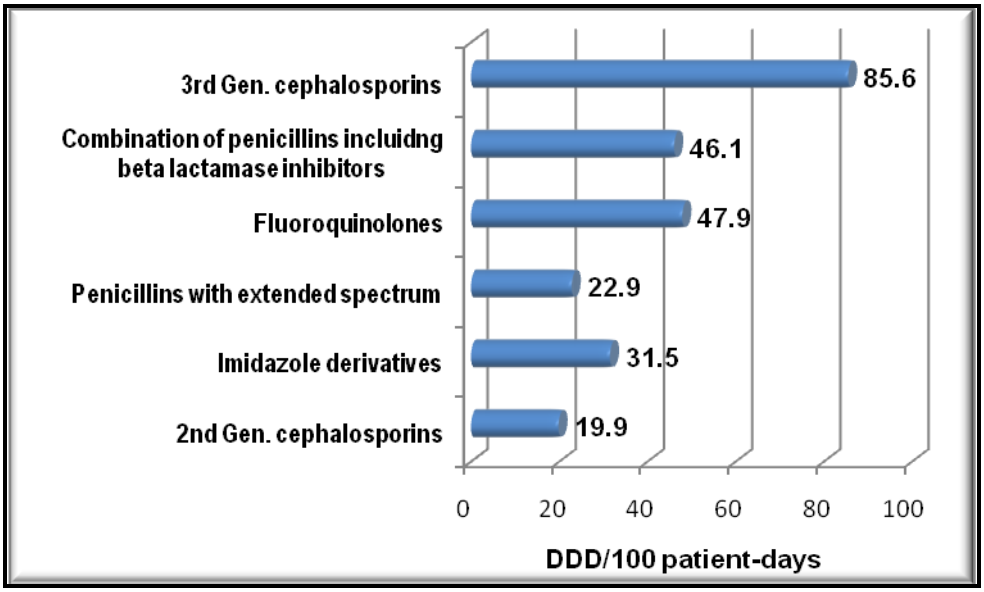
The total antibiotic use density in the ICU during the study period was 287.9 DDD/100 patient-days (Table 4).

Table 4: Antibiotic use Density according to DDD/100 patient-days along with ATC code.

S No.	Antibiotic Agent	ATC code	DDD value (Gm)	DDD/100 pt-days
1	Ceftriaxone	J01DD04	2	63.082
2	Metronidazole	J01XD01	1.5	31.541
3	Ciprofloxacin	J01MA02	0.5	28.387
4	Amoxicillin + Clavulanic acid	J01CR02	3	25.779
5	Piperacillin +Tazobactam	J01CR05	14	20.321
6	Cefuroxime	J01DC02	3	19.871
7	Levofloxacin	J01MA12	0.5	19.556
8	Cefexime	J01DD08	0.4	18.924

ISSN: 0975-8585

Figure 4: DDD/100 patient-days of commonly used antibiotic groups in medicine ICU



The six most prescribed groups of antibacterial drugs were, in decreasing order: third generation cephalosporins, fluoroquinolones, combination of penicillins including beta lactamase inhibitors, imidazole derivatives, penicillin with extended spectrum, and second generation cephalosporins. These drugs account for 76.1% of average usage of antibacterials during the period of study.

Considering each antibacterial agent individually in terms of their DDD_{100} values, the most used were Ceftriaxone (63.08), Metronidazole (31.54), Ciprofloxacin (28.39), Amoxicillin + Clavulanic acid (25.78), Pipperacillin + Tazobactum (20.32), Cefuroxime (19.87) and Levofloxacin (19.55).

DISCUSSION

The periodic evaluation of antibiotic usage in ICU setting is of utmost importance for providing information to health care professionals as well as policy makers for improving rational use of antibiotics. In this study, we have analysed pattern and consumption of antibiotics in patients admitted to medicine ICU.

A total of 610 patients were admitted during the six month study period. A study from north India [10] in a tertiary care hospital with 12 bedded ICU stated to manage approximate 250-300 patients annually. This comparison suggests comparative higher patient load in the tertiary level rural hospital of central India.

In a study from the United States [11], the mean LOS of the patients was 5.2 ± 9.8 days and the overall mortality rate was 33%. In our study there was no significant decrease in the mean age of survivors compared to non survivors unlike in the American study [11]. Our mortality rate and mean LOS was less than that reported in the American study but since the

illness pattern, treatment protocols and economic conditions would be different, comparison becomes difficult.

Mean ± SD number of drugs prescribed in the ICU was 6.3 ± 2.1. In a study reported from a trauma ICU [12], mean ± SD number of drugs was 9.1 ± 6.5. In another study [11] the number was 12.1 ± 7.6. The average number of drugs in our study was less than or comparable to that reported in other studies. The average number of drugs should be kept as low as possible to minimize the risk of drug interactions, development of bacterial resistance and hospital costs [13].

The utilization of antibiotics was 287.9 DDD/100 patient-days. The utilization of third generation cephalosporins, fluoroquinolones, combination of penicillins including beta lactamase inhibitors were 85.6, 47.9, and 46.1 DDD/100 patient-days respectively. In a study reported from 35 German ICUs [14], the total antibiotic usage was 133.7 DDD/100 bed-days; the most commonly used antibiotic group was penicillin with a beta-lactamase inhibitor followed by quinolones and second generation cephalosporins.

Blood and sputum were the most common specimens sent for culture and sensitivity testing which is similar to study done in Nepal [15]. Testing for culture and sensitivity was done in 25.1 % of patients in our study which is less in comparison to previous mentioned study [10] in which 39.4% of patients were tested.

Bacterial resistance to antibiotics has emerged as an important factor influencing patient mortality and morbidity. ICUs are frequently associated with the emergence and spread of bacterial resistance resulting from multiple factors, including severity of illness, need for prolonged hospitalization and frequent use of broad-spectrum antibiotics.

External control over the use of antibiotics in the ICU and antibiotic cycling (scheduled rotation of workhorse antibiotics) has been suggested as strategies to reduce antibiotic resistance [16]. Management teams consisting of infectious disease specialists, intensive care specialists, pharmacologists/pharmacists and microbiologists may be helpful. Knowledge of antibiotics previously received by the patient and of local trends in antibiotic resistance will be useful.

Limitations of this study were:

(1) Durations of study for six months only.
(2) The study was retrospective so we were unable to correlate the antibiotic use pattern with severity of patient's illness.
(3) Use of prophylactic antibiotic therapy was not differentiated.
(4) Cost analysis has not been carried out.

Longitudinal surveillance of ICU drug use should be taken up to create a drug utilization database and to analyze and compare future trends in drug utilization.

To control excessive antibiotic use and the development of antibiotic resistance the most indicated strategy would be a multidisciplinary approach involving cooperation between infection control, nursing, pharmacy and medical staffs. Additional interventions such as post graduate training programmes and elaborations of local guidelines could be beneficial. These programs should focus on promoting expenses and infectious control, with rational antibiotic prescription and utilization aimed at minimizing the future emergence of bacterial resistance.

REFERENCES

[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] Roder BL, Nielsen SL, Magnussen P et al. J Antimicrob Chemother 1993; 32:633–642.
[3] Niederman MS. Crit Care Med 2003; 31:608- 16.
[4] Kollef MH. Crit Care 2001; 5:189-95.
[5] Pulcine C, Pradier C, Samat-Long C, Hyvernat H et al. J Antimicrob Chemother 2006; 57:546- 50.
[6] Dieckhaus KD, Cooper BW. Crit Care Clin 1998; 14:55-70.
[7] John JF Jr, Fishman NO. Clin Infect Dis 1997; 24:471–85.
[8] World Health Organization's strategy to contain resistance to antimicrobial drugs. Rev Panam Salud Publica. 2001; 10(4):284-94.
[9] Anatomical Therapeutic Chemical (ATC) classification index with Defined Daily Doses (DDDs). Oslo (Norway): WHO Collaborating Centre for Drug Statistics Methodology. 2010.
[10] Afzal Azim, Mayank Dwivedi, Bhaskar Rao P, Baronia AK, Singh RK, Prasad KN et al. J Med Microbio 2010; 59:955–60.
[11] Smythe MA, Melendy S, Jahns B, Dmuchowski C. Crit Care Med 1993; 21:1319-23.
[12] Boucher BA, Kuhl DA, Coffey BC, Fabian TC. Am J Hosp Pharm 1990; 47:805-10.
[13] Stratton CW 4th, Ratner H, Johnston PE, Schaffner W. Clin Ther 1993; 15 A:12-20.
[14] Meyer E, Jonas D, Schwab F, Rueden H, Gastmeier P, Daschner FD. (SARI) Infection 2003; 31:208-15.
[15] Shankar PR, Partha P, Dubey AK, Mishra P, Deshpande VY. Kathmandu University Medical Journal 2005; 3[2(10)]:130-7.
[16] Kollef MH. Crit Care Med 2001; 29(4):135-142.