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ANALYSIS OF DRUG UTILIZATION PATTERN AMONG HYPERTENSIVE PATIENTS ADMITTED TO MEDICAL INTENSIVE CARE UNIT OF A TERTIARY CARE HOSPITAL

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ABSTRACT

Aims and Objectives: To evaluate the drug utilization pattern among hypertensives and to calculate the Defined Daily Dose (DDD) for commonly used drugs in Medical Intensive Care Unit (MICU) of a tertiary care hospital. **Materials and Methods:** Retrospective medical record analysis was performed in patients with hypertension admitted in MICU between 1st January 2012 and 30th March 2012. The relevant data were collected in a preformed proforma. The drugs were classified according to the Anatomical Therapeutic Chemical classification (ATC) and the drug utilization was measured in DDD/100 bed-days. **Results:** Cerebrovascular accident was the most common cause for admission. Parenteral preparations (56.89%) constituted the largest share among all the drugs prescribed. Furosemide- C03CA01 with DDD 5.02 was the most commonly prescribed parenteral drug (12.12%). Amlodipine-C08CA01 with DDD 10.53 was the most commonly prescribed oral drug (11.27%). The average duration of MICU stay was 5.41 ± 4.39 days and the average number of drugs prescribed per patient was 9.41 ± 3.10. Antihypertensive drugs were prescribed in 89.19% of patients. Furosemide was the most commonly prescribed drug (35.29%) followed by Amlodipine (22.06%), Ramipril (7.35%), Prazocin (5.88%) and Metoprolol (5.88%). **Conclusion:** The present study shows several diagnostic conditions for admission in MICU and a variety of drugs utilized from various drug classes. Rational utilization pattern of antihypertensive drugs was observed. Diuretics and Calcium channel blockers (CCBs) were the most often used drug classes. Studies of this type may provide a framework for continuous monitoring of prescription pattern in hypertensive in-patients of MICU.

KEYWORDS: Drug Utilization, Hypertension, Medical Intensive Care Unit, Anatomical therapeutic chemical classification, Defined daily dose system.

INTRODUCTION

Hypertension (HTN) is an important public health challenge in both developing and developed countries resulting in high mortality and morbidity in today's world. Socio-economic, behavioral and nutritional and public health issues have also led to increase in cardiovascular disease (CVD), including stroke and myocardial infarction throughout the world.[1] A surplus of new drugs is now available, leading to better quality of life for these patients. Number of drugs in various combinations is generally used for effective long-term management.[2-4] Drug utilization studies, which evaluate, analyze the medical, social and economic outcomes of the drug therapy, are more significant and observe the prescribing attitude of physicians with the aim to provide drugs rationally.[5]

Drug utilization study is an important tool to study the clinical use of drugs in populations and its impact on health-care system.[6, 7] The medical intensive care unit (MICU) is a setting where the multiple medications are prescribed to patients. Periodic evaluation of drug utilization in MICU is necessary for optimization of health care system, proper use of resources and making prescription policy.[8]

The assumed average maintenance dose per day for a drug used for its main indication in adults is called defined daily dose (DDD). Use of DDD is an important tool to compare the drug utilization among different clinical setups within a country and between different countries. DDD/100 bed-days provide a rough estimate of drug consumption in hospital inpatients and it is a fixed unit of measurement independent of formulation and price.[9, 10] In the present study, we have evaluated the drug utilization pattern among hypertensives and calculated the DDD for commonly used drugs in MICU of a tertiary care hospital.

MATERIALS AND METHODS

This was a retrospective medical record study conducted after prior permission from Institutional Ethics Committee, S S Institute of Medical Sciences & Research Centre, Davangere, Karnataka, India. The medical records of patients with hypertension with or without diabetes mellitus admitted in MICU between 1st January and 30th March 2012 were analyzed. Data were collected for age, gender, diagnosis, duration of MICU stay, laboratory investigations and treatment provided during the stay in MICU.

Data were analyzed for demographic variables, indication of admission in MICU and systems involved, duration of MICU stay, total number of drugs prescribed per patient, proportion of common group and particular drugs used, use of fixed dose combinations (FDCs), use of generic and brand names, use of oral and parenteral formulations, use of different antihypertensives, antimicrobials and other common drugs. The drugs were classified according to the Anatomical Therapeutic Chemical classification based on their chemical, pharmacological and therapeutic properties. The drug utilization was measured in DDD/100 bed-days.[11]

DDD/100 bed-days were calculated using the following equation:

$$\text{DDD/100 bed-days} = \frac{\text{Total dose in mg during study period} * 100}{\text{DDD of drug} * \text{study duration (days)} * \text{bed strength} * \text{Avg. bed occupancy rate}}$$

STATISTICAL ANALYSIS

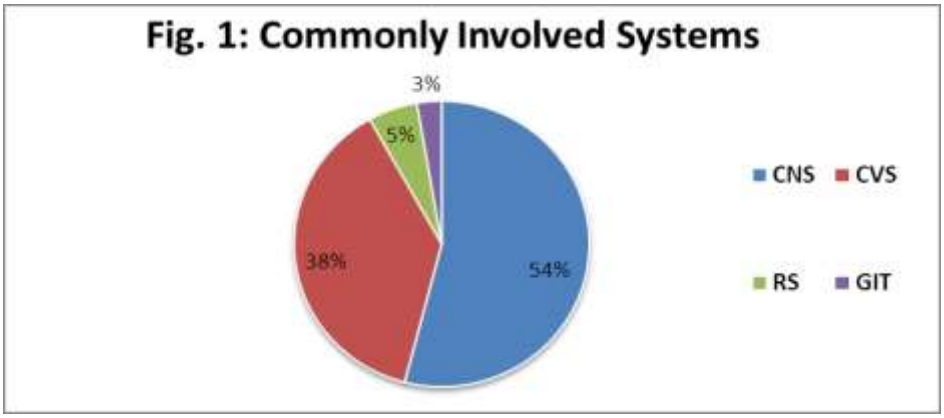
Descriptive analysis of the data collected was done by Microsoft Excel software and results were expressed as mean ± standard deviation and percentage comparison.

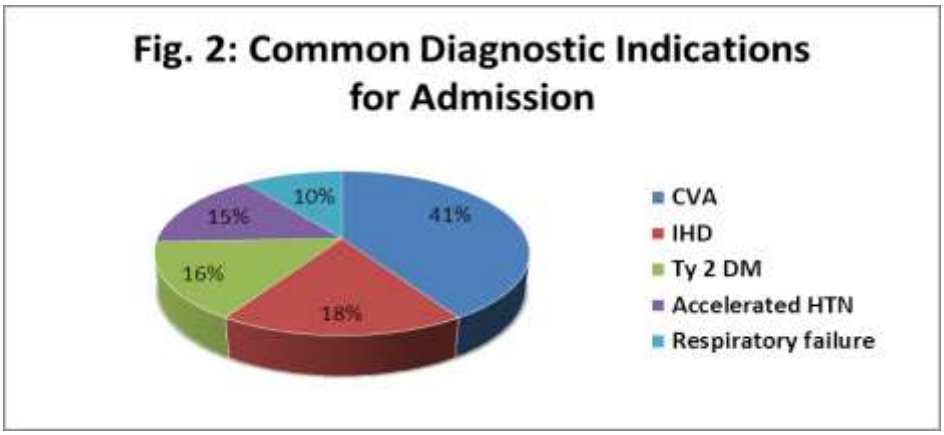
RESULTS

A total of 115 in-patient case sheets of MICU were scrutinized between 1st January and 30th March 2012. In our MICU, bed strength was 15 and average bed occupancy rate was 1.28 during the study period.

Out of the total 115 admitted patients, 37 were hypertensives. Among them 29 were both hypertensive and diabetics (78.38%) and 8 were only hypertensives (21.62%). The mean age of admitted patients was 56.62±13.39 years and all were males.

Central nervous system was the most commonly involved system followed by cardiovascular, respiratory and gastro intestinal system **[Fig. 1]**. Common diagnostic indications for admission were cerebrovascular accident (CVA), ischemic heart disease (IHD), type 2 diabetes mellitus (Ty 2 DM), accelerated hypertension and respiratory failure.





The average duration of MICU stay was 5.41 ± 4.39 days. A total of 348 drugs (56.89% parenteral, 38.21% oral formulations, 20.68% generic and 8.33% FDCs) **[Table 1]** were prescribed in all patients. The average number of drugs prescribed per patient was 9.41 ± 3.10 and 97.29% cases were given five or more drugs.

Table 1: Type of Formulations Prescribed.

TYPE OF PREPARATION	PRESCRIPTIONS (%) N=348
Parenteral	56.89%
Oral	38.21%
Other formulations	4.88%
Fixed dose combinations (FDCs)	8.33%

Table 2: Commonly Prescribed Parenteral drugs.

DRUG NAME	PERCENTAGE	ATC CODE	PHARMACOLOGICAL GROUP	DDD PER 100 BED DAYS
Furosemide	12.12%	C03CA01	Loop diuretics	5.02
Pantoprazole	11.61%	A02BC02	Proton pump inhibitor	3.04
Mannitol	10.10%	B05BC01	Osmotic diuretic	2.29
Ceftriaxone	7.57%	J01DD04	Cephalosporins	3.69
Insulin	7.07%	A10AC01	Insulin & analogues	2.78

Table 3: Commonly Prescribed Oral drugs.

DRUG NAME	PERCENTAGE	ATC CODE	PHARMACOLOGICAL GROUP	DDD PER 100 BED DAYS
Amlodipine	11.27%	C08CA01	Calcium channel blocker	10.53
Clopidogrel	11.27%	B01AC04	Antiplatelet drug	3.67
Atorvastatin	9.77%	C10AA05	Statins	4.32
Aspirin	4.51%	B01AC06	Non-steroidal anti-inflammatory drugs(NSAIDs)	2.50

Table 4: Commonly Prescribed FDCs.

FIXED DOSE COMBINATIONS	NO. OF CASES, n=29 (%)
Ipratropium bromide + Salbutamol	7 (24.14%)
Vitamins & Minerals	6 (20.69%)
Clopidogrel + Aspirin	5 (17.24%)
Piperacillin + Tazobactum	5 (17.24%)
Furosemide + Spirinolactone	2 (6.89%)

Furosemide was the commonly prescribed parenteral drug followed by pantoprazole. Among oral preparations, amlodipine was most commonly prescribed. Among FDCs, Ipratropium bromide + Salbutamol (Duolin), Vitamins & Minerals (Nurite), Clopidogrel + Aspirin (Clopitab A) and Piperacillin + Tazobactum (Tazact) were commonly prescribed **[Table 2, 3, 4].**

Total 242 (69.54%) and 185 (53.16%) drugs were prescribed from National and WHO Essential Drug lists, respectively.

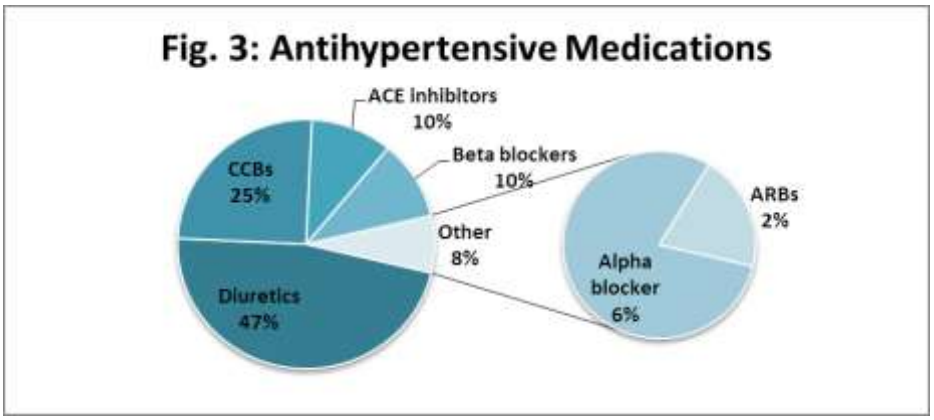
Table 5: Commonly prescribed drugs not included in National List of Essential Medicine-2011 of India.

DRUG NAME	PERCENTAGE
Rabeprazole	3.72%
Budesonide	2.01%
Ramipril	2.01%
Prazocin	1.61%

Table 6: Commonly prescribed drugs not available in WHO Essential Medicine List, 2011.

DRUG NAME	PERCENTAGE
Pantoprazole	9.24%
Clopidogrel	6.02%
Atorvastatin	5.22%
Tramadol, Midazolam, Enoxaparin sodium, Labetalol	0.80%

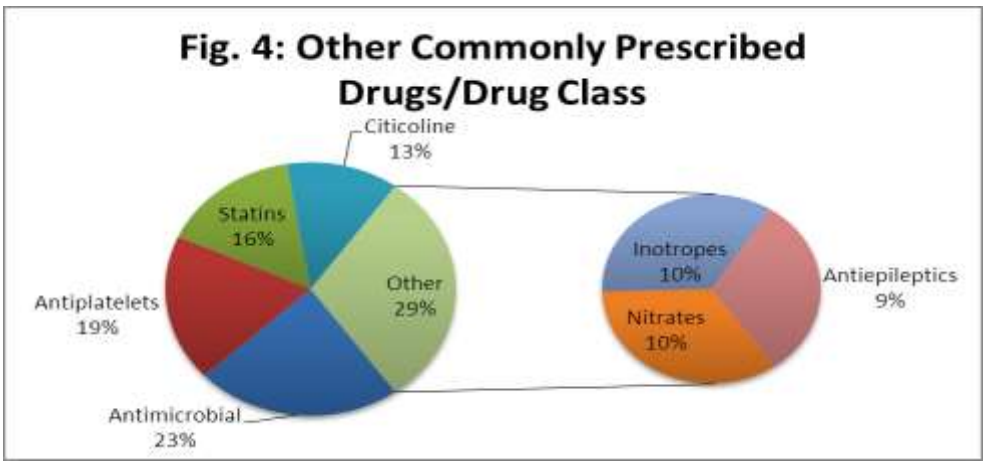
Antihypertensive drugs were prescribed in 89.19% patients [**Fig. 3]** among them 60.61% patients were prescribed with two or more drugs.



Among them, Furosemide (Loop diuretic) was the most commonly prescribed drug (35.29%) followed by Amlodipine (CCB) (22.06%), Ramipril (Angiotensin Converting Enzyme inhibitor) (7.35%), Prazocin (Alpha blocker) (5.88%) and Metoprolol (Beta blocker) (5.88%). Antidiabetic medications were prescribed to 45.95% patients, among them most were given subcutaneous insulin preparations (94.12%).

At least one antimicrobial drug was prescribed in 22 (59.46%) cases. Average number of antimicrobials prescribed per patient was 0.86 ± 0.89. Total 14 different types of antimicrobials were used. The four most commonly used antimicrobial classes were Cephalosporins (71.87%), FDC of Piperacillin + tazobactum (12.5%), Aminoglycosides (6.25%) and Fluoroquinolones (6.25%).

Antiplatelets (aspirin and clopidogrel) were prescribed to 48.65% of patients and statins were prescribed to 40.54% patients. Other commonly prescribed drugs/drug class were Citicoline, Nitrates, Inotropes and Antiepileptics **[Fig. 4]**.



DISCUSSION

Total 115 cases admitted in 15 bedded MICU of a tertiary care hospital over a period of 3 months were evaluated. Among them 37 were hypertensives.

Male preponderance (100%) was observed. The mean age of admitted patients was 56.62±13.39 years which is similar to a study done by Solanki et al[1] (56.74±11.23 years). The average duration of hospital stay per patient was 5.41 ± 4.39 days which is comparable to a study done by Jhaveri et al [11] (5.07 days) and John et al[12] (6.22 ± 3.3 days).

Apart from Hypertension, Cerebrovascular accident (43.24%), Ischemic heart disease (18.92%) and Diabetes mellitus (16.22%) were the other major comorbid conditions. Comorbidity increases the total burden of illness in a patient and also influences clinical and economic outcomes.[13]

The mean number of drugs received by patients in the present study (9.41 ± 3.10) was comparable to John et al[12] (11.6 ± 2) and Jhaveri et al[11] (9.37) but higher compared to details from Smythe et al study in 1993 [14] (12.1 ± 7.6) and Williams et al, 2011[15] (6.23 ± 2.73) indicating increase in drug utilization. Five or more drugs were prescribed in 97.29% cases, similar to John et al[12] (100%) and Jhaveri et al[11] (95%). It may be related with multiple comorbidities. Use of five or more drugs concomitantly which could augment drug interactions and drug related problems is called 'Polypharmacy'.[16] It is essential to stabilize the number of drugs and effective pharmacotherapy as it is difficult to treat patients in the ICU with multiple comorbidities, who require treatment for specific condition as well as for prophylaxis.

Furosemide (C03CA01) with DDD 5.02 was found to be the most frequently prescribed parenteral drug. Though furosemide is a strong diuretic it is a weak antihypertensive, fall in blood pressure depends on reduction in plasma volume and cardiac output. But, in this study many patients had associated oedema, may be due to CVA, heart failure or renal failure. Loop diuretics are used irrespective of etiology of oedema.[17] This could be the reason for extensive utilization of furosemide.

Amlodipine (C08CA01) with DDD 10.53 was found to be the most frequently prescribed oral drug, which was comparable to a study by John et al.[12] Critically ill patients are generally

more prone to renal failure secondary to sepsis, CCBs are preferred to ACEIs to avoid hyperkalemia and worsening of renal function.

Total of 8.33% patients received one or more FDCs, very less compared to Jhaveri et al[11] (17.87%). FDCs can enhance patient compliance and reduce packaging and shipping cost in developing countries, but the exact benefits are not clear.[18] It is difficult to titrate the dose of a single drug if desired in any stage of pharmacotherapy.[19]

In our study 71.55% drugs were prescribed from National and WHO Essential drug lists, which was much higher than the similar study by Jhaveri et al[11] (<50%), suggesting improved adherence to these lists in our set up. However, in the present study 79.31% drugs were prescribed by brand name and 20.68% drugs were given by generic name, making it apparent that more than 2/3rd of drugs were being prescribed by brand name.

In our study, hypertension was associated with various concurrent diseases and its complications, requiring polypharmacy. The mean number of antihypertensive prescribed were 11.33 ± 11.47. Among the antihypertensive drugs, Furosemide (Loop diuretic) was the most commonly prescribed drug (35.29%) followed by Amlodipine (CCBs) (22.06%), Ramipril (ACEIs) (7.35%), Prazocin (α blocker) (5.88%) and Metoprolol (β blocker) (5.88%). Loop diuretics are particularly preferred in patients with severe HTN especially with cardiac and renal insufficiency.[19] Our findings were in dissonance with study conducted by Solanki et al in out patients setting who reported ACEIs (79.66%) were the most commonly prescribed drug followed by Atenolol (49.66%), Amlodipine (33.83%), Furosemide (17%) and Metoprolol (4.66%).[1] Another study conducted by Jaiprakash et al,[20] showed Beta blockers (45%) were used more often followed by calcium channel blockers (25%). This difference might be due to the P-drug concept which holds good here, i.e., physician's choice with relation to the characteristics of patients, their concurrent illness, as well as the availability of medicines.[19]

Combination therapy is generally required for adequate control of HTN. Hence, in the present study, it is observed that multiple drug therapy (60.61%) was more common than single drug therapy (39.39%) which is comparable to Solanki et al,[1] 66.84% and 33.16% respectively. Moreover, combination therapy seems to be a rational approach to reduce the cardiovascular mortality.[21]

Percentage of antimicrobial prescriptions (59.46%) in our study was less compared to a study done by John et al[12] (83%). Cephalosporins (71.87%) were the most commonly used antimicrobial similar to John et al[12] study (69.13%) and Usluer et al[22] study (47.8%), but differed from Shankar et al[23] study in which penicillins were the commonest antimicrobial drug class prescribed. Cephalosporins are commonly prescribed due to their relatively lower toxicity and broad spectrum of activity. Among them third generation cephalosporins, i.e., ceftriaxone (65.22%) was the most commonly used antimicrobial, as it has longer duration of action and high efficacy in a wide range of serious infections.[17]

In our study, Aspirin was also commonly used (48.65%) in low dose for treatment and prevention of IHD, similar to a study by Jhaveri et al.[11] Statins (40.54%) were also commonly used which is justifiable with the total number of patients with cardiovascular disease.

This was a 3 months study, which is one of the limitations, longer duration study may provide better information regarding utilization pattern. As it was a retrospective study, it was not possible to assess the rationality and quality of prescriptions. The findings can only be generalized to tertiary care hospital in a developing country. Line of treatment and selection of drugs varies from physician to physician and the study provides no data for the same.

CONCLUSION

To conclude, several diagnostic conditions for admission and a wide variety of drugs were utilized from various drug classes. The present study provides a framework for continuous monitoring of prescription pattern in hypertensive in-patients of medical ICU. Combination therapy for treatment of hypertension seems to be a rational approach. Prescribing guidelines for treatment of various comorbidities is required to reduce the prevalent polypharmacy. Further studies are required from time to time in drug utilization research to ensure the optimum use of drugs.

REFERENCES

1. Solanki KC, Mistry RA, Singh AP, Jadav SP, Patel NM, Trivedi HR. Drug utilization study of anti-hypertensive drugs and their adverse effects in patients of a tertiary care hospital. J Clin Exp Res, 2013; 1: 58-67.

2. Hansson L, Dahlof B, Gudbrandsson T, Hellsing T, Kullman S, Kuylenstierna J. Antihypertensive effect of felodipine or hydralazine when added to beta-blocker therapy. J Cardiovasc Pharmacol, 1988; 12: 94-101.
3. Kjeldsen SE, Farsang C, Sleigh P, Mancia G. World Health Organization; International Society of Hypertension. 1999 WHO/ISH hypertension guidelines-highlights and esh update. J Hypertens, 2001; 19: 2285-8.
4. Ramsay LE. British Hypertension Society Guideline for hypertension management: summary. Br Med J, 1999; 319: 630-5.
5. Tiwari H, Kumar A, Kulkarni KS. Prescription monitoring of anti-hypertensive drug utilization at the Punjab University Health Centre in India. Singapore Med J, 2004; 45(3): 117-20.
6. Shankar PR, Upadhyay DK, Subish P, Bhandari RB, Das B. Drug utilisation among older inpatients in a teaching hospital in Western Nepal. Singapore Med J, 2010; 51: 28–34.
7. Sachdeva PD, Patel BG. Drug Utilization Studies- Scope and future perspectives. Int J Pharm Biol Res, 2010; 1: 11-7.
8. Patel KM, Barvaliya JM, Patel KT and Tripathi BC. Drug Utilization Pattern in Critical Care Unit in a Tertiary Care Teaching Hospital in India. Int J Crit Illn Inj Sci, 2013; 3(4): 250-5.
9. Oslo: WHO Collaborating Centre for Drug Statistics Methodology; 2002. WHO Collaborating Centre for Drug Statistics Methodology. Guidelines for ATC Classification and DDD Assignment.
10. Oslo: WHO Collaborating Centre for Drug Statistics Methodology; 2002. WHO Collaborating Centre for Drug Statistics Methodology. ATC index with DDDs.
11. Jhaveri NB, Patel KT, Barvaliya JM and Tripathi BC. Drug Utilization Pattern and Pharmacoeconomic analysis in geriatric medical in-patients of a tertiary care hospital of India. J Pharmacol Pharmacother, 2014; 5(1): 15-20.
12. John JL, Devi P, John J, Guido S. Drug Utilization Study of Antimicrobial Agents in Medical Intensive Care Unit of a Tertiary Care Hospital. Asian J Pharm Clin Res, 2011; 4(2): 81-4.
13. De Rooij SE, Abu-Hanna A, Levi M, et al. Factors that predict outcome of intensive care treatment in very elderly patients: a review. Crit Care, 2005; 9: 307-14.
14. Smythe MA, Melendy S, Jahns B, et al. An exploratory analysis of medication utilization in a medical intensive care unit. Crit Care Med, 1993; 21(9): 319-23.

15. Williams A, Mathai SA, Phillips SA. Antibiotic prescription patterns at admission into a tertiary level intensive care unit in Northern India. J Pharm Bioall Sci, 2011; 3: 531-6.
16. Viktil KK, Blix HS, Moger TA, et al. Polypharmacy as commonly defined is an indicator value in the assessment of drug-related problems. Br J Clin Pharmacol, 2007; 63(2): 187-95.
17. Tripathi KD. Essentials of Medical Pharmacology. 7th ed. New Delhi: Jaypee Brothers; 2013; 581: 727.
18. Connor J, Rafter N, Rodgers A. Do fixed-dose combination pills or unit-of-use packaging improve adherence? A systemic review? Bull World Health Organ, 2004; 82: 935–9.
19. Sharma HL, Sharma KK. Principles of Pharmacology. 2nd ed. New Delhi: Paras Medical Publisher; 2013; 265: 106.
20. Jaiprakash H, Vinotini K, Vindiya, Vsalni, Vikneshwara, Vigneswaran, Vinosha, Min CV. Drug Utilization Study of antihypertensive drugs in a clinic in Malaysia. Int J Basic Clin Pharmacol, 2013; 2(4): 407-10.
21. Mancia G, Backer GD, Dominiczak A, et al. "2007 ESH-ESC practice guidelines for the management of arterial hypertension: ESH-ESC Task Force on the management of arterial hypertension". Eur Heart J, 2007; 28: 1462-536.
22. Usluer G, Ozgunes I, Leblebicioglu H. A multicenter point-prevalence study: antimicrobial prescription frequencies in hospitalized patients in turkey. Ann Clin Microbiol Antimicrob, 2005; 4: 16.
23. 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, 2005; 3: 130-7.