Original Article

Cephalosporin utilization in the inpatient wards of a teaching hospital in western Nepal

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Objective and rationale: Information on the utilization of cephalosporins is lacking in hospitals in western Nepal. The present study was carried out to obtain information on the demographic characteristics, cephalosporin prescribing patterns, sensitivity patterns of commonly isolated microorganisms, mean ± SD cost of drugs per patient and the cephalosporin utilization in defined daily dose (DDD)/100 bed-days.
Methods: A retrospective analysis of the case records of patients admitted to the inpatient wards of the Manipal Teaching Hospital (a tertiary care hospital in Pokhara, Nepal) and prescribed a cephalosporin during the study period (1.11.2003 to 29.02.2004) was carried out. The median length of stay and cost of the drugs prescribed during the stay was calculated. The frequency of prescribing of other antibiotics coprescribed with cephalosporins was noted.
Results: 252 patients (2.56% of total patients) were prescribed cephalosporin. The median length of stay was 9 days. One hundred eighteen patients (46.8%) were prescribed cephalosporin for prophylaxis and 30 patients (11.9%) for bacteriologically proven infections. *E.coli, Klebsiella spp., S.aureus, Acinetobacter spp., P.aeruginosa, P.vulgaris* and *Enterococcus spp.* were the common organisms isolated and were generally sensitive to the prescribed cephalosporins. Mean ± SD cost of drugs per hospital admission was 34.78 ± 26.06 US$ and cephalosporins contributed to 51.56% of the total drug costs. Cephalosporin utilization was 4.6 DDDs/100 bed-days. Metronidazole was the most commonly coprescribed.
Conclusions: The use of cephalosporins was lower than that reported in the literature. Antibiotic use policies for postoperative prophylaxis and infection control policies for the wards are required.

Introduction

Drug utilization is defined as the marketing, prescription and use of drugs in a society with special emphasis on the resulting social and medical consequences.[1] Antimicrobials are among the class of drugs with the most potential impact on preventable mortality in developing countries.[2] Antimicrobial resistance is emerging as a complex problem driven by many interconnected factors especially the use and misuse of antimicrobials.[3]
Many patients believe that newer and expensive antibiotics are more effective than older agents; this belief is shared by some prescribers and results in unnecessary use of newer agents.[3] This practice causes unnecessary health care expenditure and encourages the development of resistance. Cephalosporins are a commonly used group of antibiotics in hospitals and health care facilities around the world.[4, 5, 6, 7] In the developed countries though the use of older cephalosporins is declining, that of the newer generations has increased.[8]
Cephalosporin drug use evaluations are well documented as being successful in modifying cephalosporin use and containing drug expenditure.[9] Unnecessary use of cefotaxime, a third generation cephalosporin led to an avoidable increase in costs in an internal medicine unit.[10] A study concluded that fourth-generation cephalosporins should be introduced into large hospitals only after careful assessment of potential benefits and in consultation with

an infectious disease specialist.[11]

The ATC (anatomic-therapeutic-chemical) classification assigns code letters and numbers to drugs.[12,13] The drugs are divided into different groups according to the organ or system on which they act and their chemical, pharmacological and therapeutic properties. The products are classified according to the main therapeutic use of the principal active ingredient. The defined daily dose (DDD) concept was developed to overcome objections against traditional units of drug consumption. The DDD for a given drug is on the basis of the assumed average use per day of the drug for its main indication in adults.[12] DDD/100 bed-days provides a rough estimate of consumption of drugs among hospital inpatients.[12,13]

Information on the utilization patterns of cephalosporins, the clinical conditions for which the drugs are prescribed and the DDD/100 bed-days of cephalosporins among hospital inpatients are lacking in hospitals in western Nepal. Hence the present study was carried out. The objectives of the study were to:

1) Obtain information on the age and sex distribution, department under which the patients were admitted, address of patients and duration of hospitalization
2) Assess the prescribing patterns of cephalosporins and other co prescribed antibiotics, measure cephalosporin utilization in DDD/100 bed-days
3) Identify commonly isolated microorganisms and their antibiotic sensitivity patterns and
4) Calculate average cost of drugs per hospital admission and the percentage of the total drug cost contributed by cephalosporins and the class of antibiotics as a whole.

Methods

A retrospective analysis of case records of all patients admitted to the inpatient wards of the Manipal Teaching hospital over a four-month period (1st November 2003 to 29th February 2004) and prescribed a cephalosporin during the study period were taken up for analysis. The case records were obtained from the Medical records department of the hospital.

The age, sex and residential address of the patients were noted. The diagnosis and the name, route and duration of use of the drugs prescribed during the period of hospital stay were recorded. The primary indication for prescribing a cephalosporin was documented. Body fluids sent for culture and sensitivity testing, the results of the test and the antibiotic sensitivity of the isolated microorganisms were recorded. Cephalosporin use was classified as for prophylaxis, bacteriologically proven infection (BPI) and non-bacteriologically proven infection (non-BPI). Primary prophylaxis refers to the prevention of an initial infection. The ASHP therapeutic guidelines were followed to define post-operative prophylaxis.[14] The use of antibiotics for clean surgical procedures with prosthetic placement and clean-contaminated surgeries was taken as use for prophylaxis. The use of antibiotics for dirty and contaminated procedures was taken as use for treatment.[14] BPI means an infection where the causative organisms could be isolated from the body fluids while non-BPI refers to infections suspected by other means without organisms being isolated. The median length of stay and mean ± SD number of drugs prescribed per patient was calculated. The cost of the prescribed course of each drug was calculated using the price list supplied by the hospital pharmacy. The mean ± SD cost of drugs per admission was calculated. The percentage of the total drug cost constituted by cephalosporins and the group of antibiotics as a whole was determined.

The drug usage of individual cephalosporins, different generations of cephalosporins and of the group of cephalosporins as a whole was calculated, using the defined daily dose (DDD) concept. The DDD/100 bed-days were used to measure cephalosporin use among inpatients using the following formula:

DDD/100 bed-days = $\frac{\text{No. of units delivered during the study period} \times 100}{\text{beds}}$ DDD (mg) x No. of days x No. of beds x Hospital occupancy index

Our study was carried out for a period of 121 days, the total number of inpatient beds was 300 and the occupancy index was 0.4. The frequency of prescribing of other antibiotics co-prescribed with cephalosporins was determined.

Results

Nine thousand eight hundred and forty-five patients were admitted to the inpatient wards during the study period. Eight hundred and forty-one patients (8.54%) were prescribed antibiotics. A total of 252 patients (2.56%) were prescribed cephalosporins. Cephalosporins were prescribed in 73 of the 2097 (3.48%) surgical inpatients, 50 of the 1726 (2.9%) patients admitted in the obstetrics and gynaecology wards and 25 of the 927 patients (2.7%) admitted in orthopedics. Among pediatric and internal medicine inpatients the percentage was 2.85% (57 of 2000 inpatients) and 1.51% (27 of the 1824 patients) respectively. The percentage among patients from other departments was 1.56%. One hundred and twenty-one patients were male. *Table 1* Shows the age distribution of the patients. Eighty-five patients (33.73%) were from Pokhara sub-metropolitan city while 65 (25.79%) were from Kaski district in which Pokhara city is situated. Ninety-nine patients (39.28%) were from the neighbouring districts while the remaining was from other locations.

Eighty-five patients were hospitalized for a time period

Table 1 Age distribution of hospital inpatients prescribed a cephalosporin during the study period

Age group (in years)	Number of patients	Percentage of total
<1	38	15.08
1-10	22	8.73
10-20	23	9.13
20-30	42	16.67
30-40	38	15.08
40-50	24	9.52
50-60	24	9.52
≥60	41	16.27

between 4 to 7 days, 48 for a period between 8 to 10 days while 72 were hospitalized for a period greater than 10 days. The median length of stay was 9 days.

Cephalosporins were prescribed for post-operative prophylaxis[14] in 106 patients (42.1%). The common surgeries for which cephalosporins were prescribed were open cholecystectomy, emergency lower segment cesarean section and internal fixation of fractures. The other common indications were laparoscopic cholecystectomy and abdominal hysterectomy. The other indications for prescribing cephalosporins were neonatal sepsis, pelvic inflammatory disease, urinary tract infections and fever under evaluation.

The mean ± SD number of drugs prescribed per patient was 7.41 ± 3.34. Antibiotics were prescribed for prophylaxis (106 for post-operative prophylaxis and 12 for medical prophylaxis) in 118 patients (46.8%) for BPI in 30 patients (11.9%) and for non-BPI in 104 patients. One hundred and fifteen specimens were sent for culture and sensitivity testing. The common specimens were blood (39), urine (24), pus (18) and sputum (12). The specimens were sent in cases where the patients were not responding to treatment, in cases of fever, tenderness or post-operative surgical site infections.

No growth was detected in 51 specimens (blood, pus and other specimens) while normal flora (sputum and throat swab) was grown in 15 specimens. Insignificant bacteriuria was detected in 11 urine specimens. Six specimens showed growth of contaminants. The common organisms isolated were *E.coli, Klebsiella spp., S.aureus, Acinetobacter spp.,*

Table 2 Cephalosporin sensitivity pattern of isolated microorganisms

Organism	No. isolated	Cephalosporin antibiotics Number sensitive/Number tested (percentage)						
		Ceftriaxone	Ceftazidime	Cefixime	Cefotaxime	Cephalexin	Cefuroxime	Cephazolin
E.coli	13	½* (50)	NT	0/2 (0)	3/7 (43)	2/7 (28)	0/1 (0)	NT
Acinteobacter spp.	5	1/1 (100)	1/3 (33)	0/1 (0)	NT	NT	1/1 (100)	NT
P.aeruginosa	4	NT	NT	NT	2/4 (50)	0/1 (0)	NT	NT
Klebsiella spp.	4	½ (50)	NT	NT	½ (50)	2/2 (100)	NT	NT
P. vulgaris	3	1/1 (100)	NT	0/1 (0)	½ (50)	0/1 (0)	0/1 (0)	NT
Enterococcus spp.	3	NT	NT	NT	NT	NT	NT	NT
S.aureus	3	NT	1/1 (100)	NT	NT	NT	1/1 (100)	1/1 (100)
Citrobacter spp.	2	1/1 (100)	NT	0/1 (0)	NT	0/1 (0)	0/1 (0)	NT

NT = Not tested. * The numerator refers to the number of cases where the organism was sensitive to the antibiotic while the denominator refers to the cases where the sensitivity test was carried out for the particular organism against the given antiobiotic

Table 3 Sensitivity pattern of commonly isolated microorganisms towards selected non-cephalosporin antibiotics

Organism	No. isolated	Antibiotics Number sensitive/Number tested (Percentage)									
		Pn	Tetra	Genta	Ampi	Amikacin	Ciprofloxacin	Amoxicl	Chlor	Cotri	Vanco
E.coli	13	NT	0/5 (0)	4/9 (44)	0/2 (0)	5/11 (45)	0/8 (0)	0/4 (0)	NT	2/3 (66)	NT
Acinetobacter spp.	5	NT	NT	¾ (75)	NT	1/3 (33)	2/3 (66)	0/1 (0)	NT	NT	NT
P.aeruginosa	4	NT	0/1 (0)	2/4 (50)	0/1 (0)	½ (50)	1/3 (33)	NT	NT	NT	NT
Klebsiella spp.	4	NT	0/2 (0)	2/4 (50)	0/4 (0)	3/3 (100)	2/4 (50)	NT	NT	NT	NT
P.vulgaris	3	NT	NT	1/3 (33)	0/1 (0)	2/3 (66)	2/3 (66)	0/1 (0)	NT	NT	NT
Enterococcus spp.	3	½ (50)	0/1 (0)	2/3 (66)	0/1 (0)	1/3 (33)	NT	NT	1/1 (100)	NT	2/2(100)
S.aureus	3	0/1 (0)	1/1(100)	3/3(100)	NT	¾ (75)	2/2 (100)	½ (50)	NT	0/1 (0)	2/2(100)
Citrobacter spp.	2	NT	NT	½ (50)	0/1 (0)	0/2 (0)	½ (50)	NT	0/1 (0)	0/1 (0)	NT

P.aeruginosa, P.vulgaris and *Enterococcus spp. Tables 2 and 3* show the sensitivity patterns of the isolated microorganisms towards cephalosporins and other antibiotics respectively.

The mean ± SD cost of drugs per inpatient was 2573.86 ± 1928.4 Nepalese rupees (34.78 ± 26.06 US$). Cephalosporins accounted for 51.56% of the total drug cost while the group of antibiotics as a whole contributed to 77.7% of the total drug cost.

Table 4 ATC Codes and defined daily dose of individual cephalosporins among hospital inpatients during the study period

Drug	ATC Code	Defined daily dose
First generation		
Cefazolin	J01DB04	0.015
Cephalexin	J01DB01	0.056
Cefadroxil	J01DB05	0.012
Total		0.083
Second generation		
Cefuroxime	J01DC02	
Oral		0.37
Parenteral		1.13
Cefaclor	J01DC04	0.016
Total		1.516
Third generation		
Cefotaxime	J01DD01	1.28
Ceftriaxone	J01DD04	1.46
Ceftazidime	J01DD02	0.11
Cefixime	J01DD02	0.15
Total		3.00
Overall Total		4.6

Table 4 shows the DDD/100 bed-days of cephalosporins as a whole and of different generations of cephalosporins and the ATC code and DDDs of individual cephalosporins. Metronidazole [80 patients (31.7%)] was most commonly co prescribed along with a cephalosporin. Other commonly co prescribed antibiotics were gentamicin [57 patients (22.62%)], ampicillin [37 patients (14.68%)], amikacin [25 patients (9.92%)], ciprofloxacin [22 patients (8.73%)] and coamoxiclav [20 patients (7.94%)]. Coamoxiclav contributed to 9% of the total drug costs.

Discussion

The age distribution of the patients revealed that a large number of patients were admitted in the age group >1 year and <60 years. Neonatal sepsis and bacterial meningitis were common conditions for use of cephalosporins in infants while in the age group >60 years they were mainly used for postoperative prophylaxis. A large number of patients were from Pokhara city and Kaski district in which Pokhara is situated. The Manipal Teaching hospital along with the western regional hospital, various district hospitals, private nursing homes and the teaching hospitals of other medical colleges serves the western development region of Nepal. The total population of the western development region is 45, 71, 013 according to the 2001 census.[15] Our hospital mainly gets patients from the western mountain and some of the western hill districts.

In our study 2.56% of patients were prescribed a cephalosporin. The percentage was lower than that reported in an Australian study where the usage of the cephalosporins, ceftriaxone and cefotaxime in the wards ranged from 22 to 67%.[16] In an Indian study, cephalosporins were prescribed in 10.92% of medical inpatients, 23.8% of surgical inpatients, 19.5% of patients admitted in the obstetrics and gynecology ward and 14.7% of pediatric inpatients.[17] In an Indian tertiary care hospital, cephalosporins were prescribed to 15.2% of patients in the Internal medicine ward and to 5.86% and 46.33% of patients in general surgery (including urology) and pediatrics respectively.[7] The use of cephalosporins in our hospital was lower in all specialities.

The use of third generation cephalosporins has been linked with infection with *Methicillin-resistant Staphylococcus aureus (MRSA), Clostridium difficile, Enterococci* and resistant gram-negative bacilli.[18,19] Periods of increased cephalosporin use have coincided with increased rates of isolation of vancomycin-resistant enterococci (VRE).[20] MRSA, Clostridium difficile and VRE were not isolated from

the patients taken up for the study.

The median length of stay was 9 days. This is comparable to that observed in an Australian study where the median length of stay ranged from 6 to 12 days.[16] We did not compare the length of stay among inpatients who were and were not prescribed cephalosporins.

In our study, cephalosporins were prescribed for post-operative prophylaxis in 44% of inpatients and for BPI in 14.68% of inpatients. In a previous study antibiotics were used for BPI in 32% of patients.[21] The percentage was also lower than the 59% reported in a previous study.[22] Culture and sensitivity testing was done in 96 patients (38.1%). In an Indian study, culture and sensitivity testing was done in 43.86% of patients prescribed cephalosporins.[7] The cost of testing may be a deterrent factor in more widespread adoption of testing. In our hospital, culture and sensitivity testing is not routinely employed and is done only in indicated persons as detailed. In many cases no growth was detected, normal flora was grown or insignificant bacteriuria was reported. These may be the reasons for the low percentage of isolation of microorganisms and the low use of cephalosporins for the treatment of BPI.

We do not have antibiotic use policies for postoperative prophylaxis in our hospital. However, the criteria suggested by the Centers for Disease Control and the Australian Therapeutic Guidelines were followed in only 26.4% of cases.[23,24] The lack of proper infection control practices in the operation theatre and the wards was a reason cited for the prolonged use of antibiotics for postoperative prophylaxis. We plan to look at antibiotic use for postoperative prophylaxis in detail in a future study.

Resistance to the commonly used antibiotics was seen among *P.aeruginosa, Klebsiella spp., P.vulgaris* and *E.coli*. This is a matter of concern. Resistance was noted towards the prescribed cephalosporins in a few instances. However, the low number of isolates makes it difficult to draw firm conclusions. The hospital is working towards implementing an antibiotic use policy and this may be helpful to contain the spread of resistant organisms.

The utilization of cephalosporins was 4.6 DDDs/100 bed-days. Fourth generation cephalosporins were not prescribed during the study period. A fourth generation cephalosporin, cefepime was approved for use by the hospital Drug and therapeutics committee in January 2004. Third generation cephalosporins were commonly used. The use of the first and second generation was lower and of the third generation was higher than that reported in a Dutch study.[25] The use of individual cephalosporins and of the class as a whole was lower than that reported in a Serbian hospital.[6] The DDD values of cefotaxime, cephalexin and ceftriaxone were lower than those reported in an Indian study.[7] The DDD values were lower than those previously reported from the Internal medicine ward of the Manipal Teaching hospital.[21]

In a previous study, in the western region, ampicillin + cloxacillin, ciprofloxacin + cefotaxime and ciprofloxacin + gentamicin were commonly used regimens for prophylaxis.[26] In a study conducted at Dharan, gentamicin was most frequently prescribed to pediatric inpatients followed by ampicillin, crystalline penicillin and cefotaxime.[27] In a pediatric hospital of Kathmandu valley, cephalosporins were the most frequently prescribed group of antibiotics.[28] In a teaching district hospital, cephalosporins were the most frequently prescribed antimicrobial and problems were noted in the use of antimicrobials.[29] However, the previous studies had not measured drug utilization in DDD/100 bed-days and so direct comparisons with our study may not be possible.

The mean ± SD cost of drugs was 34.78 ± 26.06 US$. Antibiotics contributed to 77.7% of the total drug cost. The mean ± SD cost of antibiotics was higher than those reported previously in the hospital.[21] Metronidazole, gentamicin, ampicillin, amikacin, ciprofloxacin and coamoxiclav were commonly co prescribed with the cephalosporins. Coamoxiclav contributed to 9% of the total drug costs. A detailed study on the prescribing of coamoxiclav among hospital inpatients is presently being carried out.

Our study had a number of limitations. The study was carried out for a time period of 4 months. Seasonal variations in disease pattern and antibiotic use were not taken into consideration. The number of organisms isolated on culture and sensitivity testing was low and it would be difficult to extrapolate the observed sensitivity patterns. The rationality of the use of cephalosporins was not investigated. We looked at only the drug costs incurred by the patient during the period of hospitalization and other costs were not studied.

Longitudinal studies of cephalosporin utilization in all the wards of the hospital are required. The reasons for prescribing cephalosporins and the rationality of use should be investigated in future studies.

Conclusion

The use of cephalosporins in our hospital was lower than that reported in the literature which is a welcome trend and has to be encouraged. The isolated organisms in general were sensitive to the cephalosporins used in the hospital. However, the low number of isolates makes it difficult to draw firm conclusions and further studies are required. Antibiotic use policies for postoperative prophylaxis and infection control policies for the wards are required.

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References

1) WHO. The selection of essential drugs. WHO Technical report 1977; serial no. 615:36.
2) Col NF, O'Connor RW. Estimating worldwide current antibiotic usage: report of task force 1. *Review of Infectious Diseases* 1987;**9** :232-43.
3) WHO. WHO global strategy for containment of antimicrobial resistance, 2001. WHO/CDS/CSR/DRS/ 2001.2.
4) Najera HL, Blasco CA, Sanz UM, Osinaga AE, Inchaurregui ALC. Trends in antimicrobial utilization at a Spanish general hospital during a 5-year period. *Pharmacoepidemiol Drug Saf* 2003;**12**:243-7.
5) Ansari F. Use of systemic anti-infective agents in Iran during 1997-1998. *Eur J Clin Pharmacol* 2001;**57**:547-51.
6) Jankovic SM, Slavica M, Dejanovic D. Drug utilization trends in clinical hospital center 'Kragujevac' from 1997 to 1999. *Indian J Pharmacol* 2001;**33**:29-36.
7) Sharma D, Reeta K, Badyal DK, Garg SK, Bhargava VK. Antimicrobial prescribing pattern in an Indian tertiary hospital. *Indian J Physiol Pharmacol* 1998;**42**:533-7.
8) Gould IM, Jappy B. Trends in hospital antimicrobial prescribing after 9 years of stewardship. *J Antimicrob Chemother* 2000;**45**:913-7.
9) Misan GM, Dollman C, Shaw DR, Burgess N. Cephalosporin utilization review and evaluation. *Pharmacoeconomics* 1995;**8**:100-22.
10) Palomares MJJ, Ordonez FR, Cejurdo RD. The use of cefotaxime on patients admitted to the internal medicine service of a general hospital. An analysis from the viewpoint of health economics. *An Med Interna* 1997;**14**:174-8.
11) Harbarth S, Pittet D, Gabriel V, Garbino J, Lew D. Cefepime- assessment of its need at a tertiary care center. *J Clin Pharmacol Ther* 1998;**23** :11-7.
12) WHO Collaborating Centre for Drug Statistics Methodology: Guidelines for ATC Classification and DDD assignment. Oslo 2002.
13) WHO Collaborating Centre for Drug Statistics Methodology: ATC index with DDDs 2002. Oslo 2002.
14) ASHP Therapeutic Guidelines on Antimicrobial prophylaxis in surgery. [www.**ashp** .org/bestpractices/ tg/TG_Surgical.pdf].
15) His Majesty's Government, Central Bureau of Statistics. Population monograph of Nepal Volume 1. Kathmandu, 2003.
16) Robertson MB, Korman TM, Dartnell JGA et al. Ceftriaxone and cefotaxime use in Victorian hospitals. *Med J Aust* 2002;**176**:524-9.
17) Srishyla MV, Naga Rani MA, Venkataraman BV. Drug utilization of antimicrobials in the in-patient setting of a tertiary hospital. *Indian J Pharmacol* 1994;**26**:282-7.
18) Paterson DL, Playford EG. Should third-generation cephalosporins be the empirical treatment of choice for severe community-acquired pneumonia in adults? *Med J Aust* 1998;**168**:344-8.
19) Ferguson JK. Vancomycin-resistant enterococci: causes and control. *Med J Aust* 1999;**171**:117-8.
20) Quale J, Landman D, Atwood E et al. Experience with a hospital-wide outbreak of vancomycin-resistant enterococci. *Am J Infect Control* 1996;**24**:372-9.
21) Shankar PR, Partha P, Shenoy N, Joshy ME, Brahmadathan KN. Prescribing patterns of antibiotics and sensitivity patterns of common microorganisms in the internal medicine ward of a teaching hospital in western Nepal: a prospective study. *Ann Clinical Microbiol Antimicrob* 2003;**2**:7.
22) Burke JP, Pestotnik SL. Antibiotic use and microbial resistance in intensive care units: impact of computer-assisted decision support. *J Chemother* 1999;**11**:530-5.
23) Writing group for Therapeutic Guidelines: Antibiotic. Therapeutic Guidelines: Antibiotic. 12th edition. Melbourne: *Therapeutic Guidelines Ltd;* 2003.
24) Centers for Disease Control and Prevention. Campaign to prevent antimicrobial resistance in healthcare settings. http://www.cdc.gov/drugresistance/healthcare/default.htm. Last accessed on February 16, 2005.
25) Janknegt R, Oude Lasshof A, Gould IM, van der Meer JWM. Antibiotic use in Dutch hospitals 1991-1996. *J Antimicrob Chemother* 2000;**45**:251-6.
26) Palikhe N, Pokharel A. Prescribing regimens of prophylactic antibiotic used in different surgeries. *Kathmandu University Medical Journal* 2003;**2**:216-224.
27) Rauniar GP, Rani MAN, Das BP, Singh R. Prescribing pattern of antimicrobial agents in pediatric inpatients. *Journal of Nepalgunj Medical College* 2003;**3**:34-37.
28) Palikhe N. Prescribing pattern of antibiotics in paediatric hospital of Kathmandu valley. *Kathmandu University Medical Journal* 2004;**2**:6-12.
29) Das BP, Sethi A, Rauniar GP. Antimicrobial utilization pattern in a teaching district hospital of Nepal. *Journal of Nepal Medical Association* 2004;**43**:119-124.