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# Utilization of Third Generation Cephalosporins in Multispeciality Teaching Hospital, Dehradun

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**Abstract**

*Antibiotic resistance has become a major clinical and public health problem within the life time of most people living today. The liberal use of third-generation cephalosporins in hospitals has been associated with the emergence of extended-spectrum beta- lactamases presenting concerns for bacterial resistance in therapeutics. The present study was carried out to identify the utilization of third generation cephalosporins in tertiary care teaching hospital in Dehradun. Total 250 inpatients were interviewed by using a data collection form. The study revealed that out of 250 patients, 213 were prescribed third generation cephalosporins. Ceftriaxone (46%) was most widely prescribed drug followed by cefixim (20.18%), ceftazidime (12.25), cefotaxime (8.92) and cefpodoxime (5.63). The maximum use of third generation cephalosporins was in medicine ward (39%) followed by patients in surgical (59, 28%), gynecology (36, 17%), orthopedic (18, 8%) and pediatric ward (9, 4%). The most common reasons for administration of third generation cephalosporins were high grade fever and gastrointestinal infections (26.29%) followed by respiratory tract infections (33,15.49%), injury cases (43, 20.19%), urinary tract infection (35,16.43%), skin and soft tissue infection (19,8.9%) and septicemia (04, 1.88%) and maximum patients were between the age group of 41-50 (23.47%) who were prescribed third generation cephalosporins.*
***Key words:*** *Antibiotic, Resistance, Third generation cephalosporins, Prescription, infections*

## INTRODUCTION

Appropriate use of antibiotics is central to limiting the development and the spread of resistant bacteria in hospitals and communities. Use of broad-spectrum antibiotics, in particular the third generation cephalosporins in nosocomial infections have been linked to the emergence of antibiotic resistance and increase in costs.[1] The emergence and spread of resistance are also threatening to create species resistant to all currently available agents.[2] The hospital setting is particularly conducive to the development of antibiotic resistance as patients who are severely ill, immuno-compromised or have devices and/or implants in them are likely to receive frequent courses of empirical or prophylactic antibiotic therapy.[3] Furthermore, the absence of guidelines for antibiotic use, protocols for rational therapeutics and infection control committees have led to overuse and misuse of antibiotics in different specialized units in hospitals.[1]

Overuse and misuse of antibiotics influences the prevalence and distribution of antibiotic resistance in common pathogens. Antibiotic usage is the only form of medical treatment where the choice of therapy for one patient can affect diseases suffered in the future by another, through the selection of resistant organisms followed by cross-infection to the new host.[4] Multiple drug resistance (MDR) mediated through R plasmids among Gram-negative bacteria has become a major nosocomial problem worldwide.[5] Due to multiple drug resistance to β-lactams, aminoglycosides and quinolones, antibiotic treatment of nosocomial infections caused by these bacteria is compromised.[6] Among the β-lactams, third generation cephalosporins, such as ceftazidime, cefotaxime, and ceftriaxone are routinely used in our clinical settings, and resistance to these drugs, due to β-lactamase production, is rampant.[7] The increasing resistance to third generation cephalosporins accompanied by an increasing cost burden has raised concerns about the detection, prevalence, and clinical implications of infections with *Escherichia coli* and *Klebsiella spp*. An important source of this resistance results from the production of extended-spectrum beta-lactamases (ESBLs) by bacteria.

ESBLs are modified beta-lactamase enzymes mainly derived from the ubiquitous TEM1/2 and SHV-1 plasmidmediated enzymes, which hydrolyse expanded spectrum cephalosporins to varying degrees. Many beta-lactamases result in resistance to third generation cephalosporins in *Enterobacteriaceae*. Genera such as *Enterobacter*, *Citrobacter* and *Serratia* posses chromosomal broad spectrum beta-lactamases which are normally repressed, and when induced result in resistance to third generation cephalosporins. *Klebsiella* and *E. coli* usually have the SHV- or Temtype beta-lactamases and key mutations in these results in true "ESBLs". ESBLs have received attention in the last decade because although penicillins, cephalosporins, or aztreonam appear to be susceptible in vitro, ESBL producing *E. coli* or *Klebsiella* spp. may demonstrate clinical resistance to these antibiotics leading to treatment failures. Liberal use of the third generation cephalosporins antibiotics has resulted in the ESBLs conferring resistance among *Enterobacter* [8] and *Enterobacteriacae* worldwide [9-11] compromising their clinical use.

In order to identify the utilization of third generation cephalosporins, an audit of prescriptions of inpatients was undertaken at Shri Mahant Indresh Hospital, a multispecialty teaching hospital in Dehradun, Uttarakhand.

## MATERIAL AND METHODS
### Study Site
The present study was carried out at Shri Mahant Indresh Hospital, Dehradun, which is a multispecialty teaching hospital providing both inpatient and outpatient services to people in and around Dehradun district.

### Study setting
The study was performed using prescriptions of 250 inpatients. The study was carried out in between June to August 2009. Various age group patients admitted in different wards of hospital were selected for the study. The prospective study in various patients was conducted who had received one or more course of treatment with one of the third generation cephalosporin. Patient's data such as the age, name, gender and data on prescribed drugs that include name of drug, dosage form, route of administration, most widely prescribed drugs and so on. Patient's characteristics, clinical data and laboratory investigations were obtained from the hospital records. Specific data on the category of service, concomitant disease and drug therapy, organ system with infection and third generation cephalosporins used were collected by using a customized data collection sheet in an approved manner.

## RESULTS
Out of 250 patients studied during study period, 213 were prescribed cephalosporins either alone or in combination with other antibiotics. Gender wise distribution of patients showed that, 109 patients were male and 104 patients were female accounting for 51.17% and 48.83% of total population who were prescribed cephalosporins respectively. The maximum number of patients who were prescribed 3$^{rd}$ generation cephalosporins were between the age groups of 41-50 (50, 23.47%) and 51-60 (47, 22.07%) followed by 31-40 ( 45, 21.13%) and 21-30 ( 26, 12.21%). **(Table-1).** During the study it was found that the use of third generation cephalosporins was highest in medicine ward (83, 38.97%) followed by patients in surgical (59, 27.7%), gynaecology (36, 16.90%), orthopedic (18, 8.45%) and pediatric ward (9, 4.22%). **Table-2** shows the distribution of patients according to the wards in which they were admitted.

Amongst the various reasons for administration of 3$^{rd}$ generation cephalosporins, the maximum reasons were of high grade fever and gastrointestinal infections (56, 26.29%) followed by respiratory tract infections (33, 15.49%), injury cases (43, 20.19%), urinary tract infection (35, 16.43%), skin and soft tissue infection (19, 8.9%) and septicemia (04, 1.88%). **(Table-3)**

By interpretation of data collected during study, it was found that ceftriaxone (98, 46%) was the most widely prescribed antibiotic amongst all 3$^{rd}$ generation cephalosporins followed by prescriptions of cefixim (43, 20.18%), ceftazidime (26, 12.25%), cefotaxime (19, 8.92%), cefpodoxime (12, 5.63%).**(Table-4)**

## DISCUSSION
The increasing frequency with which antibiotic resistant microorganisms are recovered from patients in hospital and community setting has been commented widely in recent years.[12,13,14] The major selective pressure driving changes in the frequency of resistance is in each case, the volume of antibiotics use.[15]

The increasing resistance problems of recent years are probably related to the overuse of broad spectrum agents such as cephalosporins.[16] The extensive use of third generation cephalosporins has caused the emergence of extended spectrum beta lactamases in gram negative bacteria worldwide.[1] More third generation cephalosporins are being widely used in hospitals for empirical and prophylactic therapy and as their use extends across the board, more organisms will develop

**Table. 1: Age wise distribution of inpatients that were prescribed 3GCs**

| Age Group ( years) | Male | Female | Total | (%) |
|---|---|---|---|---|
| 1-10 | 5 | 4 | 9 | 4.22 |
| 11-20 | 11 | 10 | 21 | 9.86 |
| 21-30 | 12 | 14 | 26 | 12.21 |
| 31-40 | 19 | 26 | 45 | 21.13 |
| 41-50 | 28 | 22 | 50 | 23.47 |
| 51-60 | 25 | 22 | 47 | 22.07 |
| 61-70 | 09 | 06 | 15 | 7.04 |
| Total | 109 | 104 | 213 | 100 |

**Table. 2: Ward wise distribution of patients that were prescribed 3GCs**

| Hospital Ward | Number of Patients (n=213) | Percentage (%) |
|---|---|---|
| Medicine | 83 | 38.97 |
| Surgery | 59 | 27.7 |
| Gynaecology | 36 | 16.90 |
| Orthopedics | 18 | 8.45 |
| Pediatrics | 09 | 4.22 |
| Other | 08 | 3.76 |

*n= Number of patients that were prescribed third generation cephalosporins*

**Table. 3: Reasons for administration of 3GCs**

| Reasons | Number of Patients | (Percentage) % |
|---|---|---|
| Fever/ GIT infection | 56 | 26.29 |
| Respiratory tract infection | 33 | 15.49 |
| Injury | 43 | 20.19 |
| Urinary tract infection | 35 | 16.43 |
| Skin and soft tissue infection | 19 | 8.92 |
| Septicemia | 04 | 1.88 |
| Others | 23 | 10.80 |
| Total | 213 | 100 |

**Table. 4: Distribution of prescriptions according to widely prescribed 3GCs**

| Third Generation Cephalosporins | Number of Prescription n= 213 | Percentage (%) |
|---|---|---|
| Ceftriaxone | 98 | 46.00 |
| Cefixime | 43 | 20.18 |
| Ceftazidime | 26 | 12.25 |
| Cefotaxime | 19 | 8.92 |
| Cefpodoxime | 12 | 5.63 |
| Ceftriaxone + Salbactun | 7 | 3.28 |
| Cefixime + Salbactum | 5 | 2.34 |
| Cefotaxime + Salbactum | 3 | 1.40 |

*n= Number of patients that were prescribed third generation cephalosporins*

resistance to them presenting the threat of antibiotic ineffectiveness in life threatening infections.

Various literatures have been reported the inappropriate use of third generation cephalosporins. Inappropriate antibiotics use has been reported from teaching hospitals in New York[17] in the surgical practice, in China[18] where inappropriate third generation cephalosporins use was an independent risk factor for significant high mortality, in Malaysia[19] for patients in medical wards and in South Africa[20] for patient in gynaecology ward. In our study we found that out of 250 patients, 213 were receiving third generation cephalosporins, which was quite inappropriate. The result of the study revealed the higher inappropriate use of ceftriaxone when used as single agent rather than in combination therapy with other antibiotics. We believe this practice may have followed from the convenience of a single daily dose by intramuscular injection particularly for ceftriaxone, which was the most frequently used third generation cephalosporin.

**CONCLUSION**

Antibiotic resistance is rapidly increasing global problem. It contributes to health and economic losses world wide. As antibiotics have important role in clinical care, thus efforts should be made to reduce the volume of unnecessary antibiotic prescribing. The present study shows the high proportion of hospitalized patients who receive antibiotics particularly broad spectrum agents like cephalosporins. In addition to their broader spectrum activity, third generation cephalosporins are widely used for empirical treatment of severe or complicated infections and for direct treatment of otherwise resistant organisms. The expanding use of these agents can promote escalating antibiotic resistance within both individual and communities. As a result, the medical profession is losing some of its most potent therapies for patients with greatest need.

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