

## Original Research Article

### Cephalosporin resistance pattern in a tertiary care hospital – An observation study

Haritha Manchi<sup>1</sup>, B L Kudagi<sup>1</sup>, Madhavulu Buchineni<sup>1\*</sup>, K. Jithendra<sup>2</sup>,  
V.Bhopal Chandra<sup>1</sup>, Rama Mohan Pathapati<sup>1</sup>, M.Rajesh Kumar<sup>1</sup> and N.Anjani Devi<sup>3</sup>

<sup>1</sup>Department of Pharmacology, Narayana Medical College, Nellore, India

<sup>2</sup>Department of Microbiology, Narayana Medical College, Nellore, India

<sup>3</sup>Narayana College of Nursing, Nellore, India

\*Corresponding author

#### A B S T R A C T

The Cephalosporin antibiotics have become a major part of the antibiotic formulary for hospitals in developing countries. The number of microbial organisms developing increasing resistance against Betalactam antibiotics. The aim of this study is to evaluate the sensitivity pattern of Cephalosporin antibiotics in tertiary care teaching Hospital. This study was conducted for a period of 6 months in a tertiary care hospital in Nellore. The clinically suspected laboratory samples were collected from the patients and subjected to culture and antibiotic sensitivity testing. Anti microbial susceptibility testing was done on Mueller Hinton agar plate by Kirby Bauer Disc diffusion method and the samples include pus, urine, blood, and sputum. The total 100 clinical samples were collected; out of them 40% are pus, 20% sputum, 10% blood and 30% of urine samples. Among the 40 Pus samples - 25 resistance, 20 Sputum samples -12 resistance, 10 Blood samples - 6 resistance, and 30 Urine samples - 16 samples have shown resistance. Third and fourth generation Cephalosporins have better sensitivity when compared to first and second generation cephalosporins and explores the emergence of sensitivity and resistance of organisms to Cephalosporins in a tertiary care hospital. Intermittent antimicrobial resistance monitoring and alternation of antibiotics were suggested to restrict further emergence of resistance.

#### Keywords

Cephalosporins,  
Antibiotics,  
antimicrobial  
resistance,  
Hospital  
antibiotic policy

## Introduction

Antimicrobial resistance (AMR), a growing public health concern where the microorganism is able to survive exposure to antibiotic treatment <sup>(1)</sup>. This is evident from the first report of vancomycin resistant Staphylococcus aureus (VRSA) from the US in 2002, Brazil in 2005, Jordan and India in

2006. Similarly, resistance was reported in the late 1980s, with vancomycin resistant Enterococci. Controlling infections is going to be a tough job in developing countries like India where infectious diseases still hold high morbidity and mortality <sup>(2)</sup>.

The Cephalosporin antibiotics have become a major part of the antibiotic formulary for hospitals in developing to affluent countries. They are prescribed for a wide variety of infections every day. Cephalosporins are a group of semi synthetic antibiotics derived from cephalosporin-C obtained from a fungus *Cephalosporium*; these are bactericidal and act by inhibition of cell wall synthesis. Cephalosporins are used to treat a wide variety of bacterial infections, such as respiratory tract infections (pneumonia, tonsillitis, and bronchitis), skin infections and urinary tract infections. They are sometimes given with other antibiotics. Cephalosporins are also commonly used for surgical prophylaxis - prevention of bacterial infection before, during, and after surgery<sup>(3)</sup> Although widely accepted as broad-spectrum antibiotics, cephalosporins are not active against all the bacteria commonly isolated in a hospital microbiology laboratory<sup>(4)</sup> Furthermore, there is an association between cephalosporin usage and the emergence of multiply-resistant organisms<sup>(5-8)</sup>

Their undoubted popularity relies upon lesser allergenic and toxicity risks as well as broad spectrum of activity. It is the latter feature; however, that encourages the selection of microorganisms that are resistant to these agents. There are long-term implications for the treatment and control of this heterogeneous group of super infections. When clinicians evaluate a septic patient, it is understandable that they choose empirical therapy with a cephalosporin whilst awaiting microbiological and other tests, since bacterial identification and antimicrobial testing usually require 24-48 h.

The broad-spectrum capability of these drugs, however, encourages rapid overgrowth of some microorganisms that are neither eliminated nor inhibited by therapy.

These organisms not only have pathogenic potential, they may also be multiply and become resistant to antibiotics.

Although widely accepted as broad-spectrum antibiotics, Cephalosporins are not active against all the bacteria commonly isolated in a hospital microbiology laboratory. Organisms that are not inhibited by Cephalosporin therapy consequently overgrow, with varying potential to cause infection. Some of these are instantly recognizable as pathogens; others, although originally regarded as commensal or of low risk status, have subsequently been shown to cause disease. Furthermore, there is an association between Cephalosporin usage and the emergence of multiple resistant organisms. Antibiotic usage patterns exert a significant influence over the rates of resistance observed in problematic multidrug-resistant nosocomial pathogens. Strict adherence to well-accepted infection control guidelines, along with caution in use of broad-spectrum antimicrobial agents, represents the best strategy for preventing the emergence and spread of multidrug-resistant pathogens.

The present study was undertaken in the department of microbiology, from where the clinical samples of different specimen were collected for studying the sensitivity of Cephalosporins that are commonly used in Narayana Tertiary Care Hospital, Chinthareddypalem, Nellore. Hence the present study explores the emergence of sensitivity and resistance of most commonly used Cephalosporins.

## **Materials and Methods**

This prospective study was conducted in the department of Microbiology, Narayana Medical College & Hospital, Nellore. Hundred hospitalized patient's samples such

as pus, urine sputum, blood, were collected. These samples were under gone to culture and sensitivity test. The study was conducted for a period of 6 months from November 2008 to April 2009.

Anti microbial susceptibility testing was done on Mueller Hinton agar plate by Kirby Bauer Disc diffusion method as recommended by Clinical Laboratory Standard Institute (CLSI)<sup>(9)</sup>. After inoculum has dried specific antibiotics discs were placed 2 cm apart from each other with sterile forceps and plate was incubated for 18-24 hours at 37°C aerobically. The zone size was measured and the susceptibility interpreted according to the reference chart provided by the manufacturer according to NCCLS standards for each organism. Antibiotic sensitivity testing method was performed by Kirby-Bauer disc diffusion method<sup>(10)</sup>.

Following cephalosporin Antibiotics were tested for the study

- (1) Cephalexin 30µg / disc
- (2) Cefotaxime 30µg / disc
- (3) Cefazolin 30µg / disc
- (4) Cefixime 5µg / disc
- (5) Ceftazidime 30µg / disc
- (6) Cefadroxil 30µg / disc
- (7) Cefoperazone 75µg / disc
- (8) Cefipime 50µg / disc ;
- (9) Cefuroxime 30µg / disc

## Result and Discussion

A total of 100 clinical samples were collected, out of them 40% are pus, 20% sputum, 10% blood and 30% of urine samples. Among the 40 Pus samples that are collected, 25 samples have shown resistance, and the remaining has shown sensitivity; Among the 20 Sputum samples collected, 12 samples have shown

resistance, where the remaining has shown sensitivity; Among the 10 Blood samples collected, 06 samples have shown resistance, and the remaining samples has shown sensitivity; Among the 30 Urine samples collected, 16 samples have shown resistance, and the remaining has shown sensitivity.

In the present study on Sensitivity of Cephalosporins, as per the above graph, First generation Cephalosporin drugs like (*Cephalexin, cefazollin, and Cefadroxyl*) has shown more resistance, than sensitivity, coming to the second generation drugs like *Cefuroxime* has shown resistance more or less equal to first generation drugs, and the third generation drugs like *Cefotaxime, Cefixime, Ceftazidime and Cefoperazone* has shown mild sensitivity than fourth generation drugs like *Cefipime*.

Microbial resistance to antimicrobials is a matter of great importance if sensitive strains are supplanted by resistant ones, then a valuable drug may become useless. Resistance may become more prevalent in a human population by spread of microorganisms containing resistance genes, and this may also occur by dissemination of the resistance genes among different microbial species. Because resistant strains are encouraged (selected) at the population level by use of antimicrobial agents, antibiotics are the only group of therapeutic agents which can alter the actual diseases suffered by untreated individuals. Prescribing colleagues will almost certainly question how just one group of antibiotics alone, within the extensive Beta-lactam class antibiotics, could be the most important driving force behind the continuing increase in resistant organisms, even allowing for broad- spectrum activity and popularity<sup>(11-13)</sup> In defence of the cephalosporin antibiotics, they provide useful activity

against a number of common pathogens, and their low toxicity reassures clinicians and obviates the need for serum levels<sup>(14)</sup> Various microorganisms of gram positive organisms like *Staphylococci aureus* and *Staphylococci epidemis*, *Staphylococcus pneumoniae*, *Streptococcus pyogens* and gram negative organisms like *Klebsiella*, *Pneumoniae*, *E.colli*, *Shigella* and other organisms like *Hemophilus influenza*, *Enterobacterea*, *Citrobacter* etc were isolated from different sample. The organisms may cause various diseases like viral fever, ulcerations, diabetic foot, peptic ulcer, meningitis, pharyngitis, otitis media, osteomyelities, urinary tract infections etc.

Cephalosporins are grouped by their spectrum of activity against antimicrobial organisms. First-generation Cephalosporins are active against most gram-positive bacteria (except *Enterococci* and *Listeria*) and have limited activity against some gram-negative organisms. Second-generation Cephalosporins have increased activity against gram-negative organisms. Cephamycins, which generally are classified with the second-generation Cephalosporins, have enhanced activity against anaerobic bacteria. The third-generation Cephalosporins have extended potency against gram-negative bacteria but are generally less active against susceptible *Staphylococci*. *Cefepime hydrochloride* is a newer semi synthetic, broad-spectrum fourth-generation Cephalosporin antibiotic. The other antibiotic in this class is *Cefpirome*.

In this prospective study, a total number of hundred samples with blood, urine, pus, sputum were collected which consists of pus 40%, sputum 20%, blood 10%, & urine 30% and among the 40 pus sample that are collected, 25 samples have shown resistant, and the remaining 15 have shown

sensitivity. Among the 20 sputum samples collected 12 samples have shown resistance were remaining 08 shown sensitivity, among the 10 blood samples collected 06 samples have shown resistance and the remaining 04 shown sensitivity, among the 30 urine sample collected 06 sample have shown resistance and remaining 16 shown sensitivity.

The total hundred samples, *Cephalexin* shown 30% sensitivity and 70% resistance, *Cefotaxime* shown 45% sensitivity and 55% resistance, *Cefozolin* shown 25% sensitivity and 75% resistance, *Cefixime* shown 40% resistance and 60% resistance, *Ceftazidime* shown 55% sensitivity and 45% resistance, *Cefadroxyl* shown 20% sensitivity and 80% resistance, *Cefoperazone* shown 35% sensitivity and 65% resistance, *Cefipime* shown equal sensitivity and resistance of about 50%, *Cefuroxime* has shown 20% sensitivity and 80% of resistance.

In a study, on invitro patterns of third generation Cephalosporins against commonly isolated gram negative pathogens at UERM memorial hospital conducted by *Ranulfo B. javelosa, et.al*, in 1988, *Ceftazidime* have shown 90.2% sensitivity, *Ceftriaxone* have shown 89.9% sensitivity and *Cefaperazone* have shown 89.8% sensitivity. But in our study, *Ceftazidime* have shown a considerably a significant sensitivity about 55%, and *Cefaperazone* have shown considerably a significant sensitivity about 35%(15). This clearly suggests that organism have become resistant with the passage of time.

In 1990 a study, *B.Mishra et al* on 70 strains of *Pseudomonas aeruginosa* isolated from clinical sample of hospital- infected cases were tested for sensitivity to *Ceftazidime*, *Cefotaxime* and *Cephazoline*, 05 strains (7%) were resistant to *Ceftazidime*, 28

(40%) to Cefotaxime and 56 (80%) to Cefazoline. Similarly in a study conducted by A.Subha, S Ananthan, 2002, has shown 95% resistance or decreases susceptibility to atleast one of the three 3<sup>rd</sup> generation cephalosporins like Ceftazidime, Cefotaxime Ceftriaxone. Where as in the present study Ceftazidime have shown 45% resistance, and Cefotaxime also showed same resistance as ceftazidime, where as Cefazolin have shown 75% of resistance<sup>(16)</sup>

A Study conducted by A.Chaudhury in 2003 on in vitro activity of Cefepirome versus three other Cephalosporins namely Cefazolin, Cefuroxime and Cefotaxime where the data collected from different clinical are like urine, pus, blood, sputum and CSF and shown the resistance of various Cephalosporins like Cefazolin 73% resistance to Staphylococci aureus and 35% resistant to coagulase negative Staphylococci.<sup>15</sup> Similarly a study conducted by Farida anjum and Asif mir 2010 on the susceptibility pattern Pseudomonas aeruginosa against various antibiotics Cefazolin has shown 99% of resistance for clinical isolates.

In present study Cefazolin have shown more or less similar resistance about 75% and 25% of sensitivity to different clinical isolates<sup>(17)</sup>

A Study conducted by A.Chaudhury in 2003, other drug Cefuroxime has shown 96% resistance to Staphylococci aureus and 37% resistance to Pseudomonas species and 75% resistance to Non Fermentative Gram Negative Bacilli (NFGNB) and 72% resistance to Enterobacteriaceae. In the same way a Study conducted by Farida anjum,Asif mir in 2010, Pseudomonas aeruginosa have shown a highest resistance to Cefuroxime (100%). Similarly in our study we have observed 80% resistance and

20% sensitivity for different organisms for Cefuroxime.

In a study by A.O.Okesola, O. Makanjuola , 2009, out of the total number of Enterobacteriaceae isolated in the study period, only 54.8% of Klebsiella species isolated were sensitive to Ceftazidime, 48.4% to Ceftriaxone and 30.7% to Cefotaxime. With Escherichia coli however, the susceptibility pattern to the 3<sup>rd</sup> generation Cephalosporins was better (65.6% were sensitivity to Ceftazidime, 62.5% to Ceftriaxone and 71.9% to Cefotaxime). In Proteus species the susceptibility pattern was generally poor to the three classes of antibiotics (50% were sensitive to Ceftazidime and Ceftriaxone, 0% to Cefotaxime.)In our study we observed Ceftazidime have shown a considerably significant sensitivity about 55% and Cefotaxime has shown a sensitivity of 45%<sup>(18)</sup>

In a study conducted by N.H.Zahani and H. Babazadeh, 2010, on antibiotic resistance of Cefipime, it has shown 75.4% of resistance, 22.4% of intermediate resistance, and 2.1% of sensitivity, but in our study, the observations were comparatively less similar, and a significant resistance to Cefipime of about 50%, was seen<sup>(19)</sup>

Conclusion if the study is first generation Cephalosporin drugs like (*Cephalexin, cefazollin, and Cefadroxyl*) has shown more resistance, than sensitivity, coming to the second generation drugs like *Cefuroxime* has shown resistance more or less equal to first generation drugs, and the third generation drugs like *Cefotaxime, Cefixime, Ceftazidime and Cefoperazone* has shown mild sensitivity than fourth generation drugs like *Cefipime*.

Finally, the study concludes that the third

and fourth generation Cephalosporins have better sensitivity when compared to first and second generation Cephalosporins. Here by,

the present study explores the emergence of sensitivity and resistance of organisms to Cephalosporins in a tertiary care hospital.

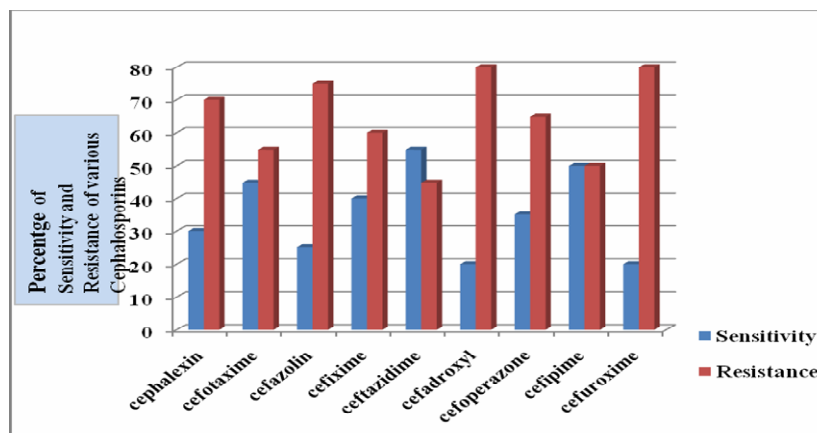
**Table.1** Sensitivity and Resistivity of samples in different Specimen

Specimen	Sensitivity	Resistance
Pus	15	25
Sputum	08	12
Blood	04	06
Urine	14	16

**Table.2** Showing the Percentage of Sensitivity and Resistance of Various Cephalosporins that are used in the study

Name of the drugs	Percentage of Sensitivity (%)	Percentage of Resistance (%)
<b>Cephalexin</b>	<b>30</b>	<b>70</b>
<b>Cefotaxime</b>	<b>45</b>	<b>55</b>
<b>Cefazolin</b>	<b>25</b>	<b>75</b>
<b>Cefixime</b>	<b>40</b>	<b>60</b>
<b>Ceftazidime</b>	<b>55</b>	<b>45</b>
<b>Cefadroxy</b>	<b>20</b>	<b>80</b>
<b>Cefoperazone</b>	<b>35</b>	<b>65</b>
<b>Cefipime</b>	<b>50</b>	<b>50</b>
<b>Cefuroxime</b>	<b>20</b>	<b>80</b>

**Figure.1**



## References

1. Raghunath D. Emerging antibiotic resistance in bacteria with special reference to India. *J Biosci* 2008; 33:593-603.
2. Gupta SK, Gupta P, Sharma P, Shrivastava AK, Soni SK. Emerging and reemerging infectious diseases future challenges and Strategy. *J Clin Diagn Res* 2012; 6:1095-100
3. Alan R. Salkind, MD, and Kavitha C. Rao, MD, University of Missouri–Kansas City School of Medicine, Kansas City, Missouri *Am Fam Physician*. 2011 Mar 1; 83(5):585-590.
4. Livermore, D. M. Mechanisms of resistance to  $\beta$ -lactam antibiotics. *Scandinavian Journal of Infectious Diseases Supplement*.1991. 78, 7–16
5. Bamberger, D. M. & Dahl, S. L. Impact of voluntary vs. enforced compliance of third-generation cephalosporin use in a teaching hospital. *Archives of Internal Medicine* 1992.152, 554–7.
6. Nicolle, L. E. Prior antimicrobial therapy and resistance of *Enterobacter*, *Citrobacter* and *Serratia* to third generation cephalosporins. *Journal of Hospital Infection* (1988) 11, 321–7.
7. Follath, F., Costa, E., Thommen, A., Frei, R., Burdeska, A. & Meyer, J. Clinical consequences of development of resistance to third generation cephalosporins. . (1987). *European Journal of Clinical Microbiology* 6, 446–50.
8. Salacata, A. & Chow, J. W. Cephalosporin therapeutics for intensive care infections. *New Horizon* 1, 1993. 181–6.
9. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial disk susceptibility tests 2006. Approved standard M2-A9. CLSI, Wayne, PA
10. Jan Hudzicki, Kirby-Bauer Disk Diffusion Susceptibility Test Protocol, American Society for microbiology. 08 December 2009, (<http://www.microbe library.org/component/resource/laboratory-test/3189-kirby-bauer-disk-diffusion-susceptibility-test-protocol>)
11. Gould, I. M. A review of the role of antibiotic policies in the control of antibiotic resistance. *Journal of Antimicrobial Chemotherapy*. 1999. A3, 459-65.
12. McGowan, J. E. Do intensive hospital antibiotic control programs prevent the spread of antibiotic resistance. 1994. *Infection Control and Hospital Epidemiology* 15, 478-83.
13. Shales D. M., Gerding, D. N., John, J. F., Craig, W. A., Bornstein, D. L., Duncan, R. A. et al. Guidelines for the prevention of antimicrobial resistance in hospitals. Society for Healthcare Epidemiology of America and Infectious Diseases Society of America Joint Committee on the Prevention of Antimicrobial Resistance. *Infection Control and Hospital Epidemiology* (1997). 18, 275-91
14. Neu H. C. Third generation cephalosporins: safety profiles after 10 years of clinical use. *Journal of Clinical Pharmacology* .1990. 30, 396-403.
15. Ranulfo B. Javelosa, Adrian C. Pena. In vitro patterns of third generation Cephalosporins against

- commonly isolated gram negative pathogens at UERM memorial hospital. *PJMID* 1989; 18(1): 34-38.
16. B.Mishra, R. Kandhari, A. Mandal, Susceptibility of *Pseudomonas aeruginosa* to newer Cephalosporins. *Indian J.Med.Microbiol* 1990; 8: 68-71.
  17. Farida Anjum, Asif Mir. Susceptibility of *Pseudomonas aeruginosa* against various antibiotics. *African journal of Microbiology reseaech* 2010; 4(10): 1005-12.
  18. A.O.Okesola, O. Makanjuola. Resistance to third-generation Cephalosporins and other antibiotics by enterobacteriaceae in western Nigeria. *American Journal of Infections diseases* 2009; 5(1): 17-20.
  19. N.H. Jazani1, H. Babazade, Z. Sabahi, M. Zartoshti. The evaluation of antibiotic resistance to Cefepime inhospital isolates of *Pseudomonas aeruginos*. *Journal of Medicine and Biomedical Sciences* 2010; 34: 2073-78.