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Superbugs against cephalosporin, observational study at tertiary care hospital in India

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Abstract
Background: The Cephalosporin antibiotics have become a major part of the antibiotic formulary for hospitals in developing countries. The numbers of bacteria developing resistance against Beta lactam antibiotics.
Objective: To evaluate the sensitivity pattern of Cephalosporin antibiotics in tertiary care teaching Hospital.
Method: This study was conducted for a period of 6 months in a tertiary care hospital in Surat. 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, semen, endotracheal tube, catheter tip and sputum.
Results: The total 685 clinical samples were collected; out of them 23.4% are pus, 14.6% sputum, 7.3% blood, 21.9% urine, faeces 5.8%, 13.1% endotracheal tube, 6.6% catheter tip and 2.9% of semen samples. Among the 160 Pus samples – 100 resistances, 100 Sputum samples -60 resistance, 50 Blood samples – 30 resistance, 150 Urine samples – 80 resistance, 50 semen samples -30 resistance, 90 endotracheal tube samples -30 resistance and 45 catheter tip -30 samples have shown resistance.
Conclusion: The study concludes that the *ceftazidime* and fourth generation Cephalosporins have better sensitivity when compared to first, second and some third generation Cephalosporins. Here by, the present study explores the emergence of sensitivity and resistance of organisms to Cephalosporins in a tertiary care hospital.

Keywords: Cephalosporin, Antimicrobial resistance (AMR)

1. Introduction
Antimicrobial resistance (AMR), a growing public health concern where the microorganism is able to survive in the presence of antibiotics [1]. 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 [2].
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 [3]. Although widely accepted as broad-spectrum antibiotics, cephalosporins are not active against all the bacteria commonly isolated in a hospital microbiology laboratory [4]. Furthermore, there is an association between cephalosporin usage and the emergence of multiply-resistant organisms [5, 8]. 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 exerted 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 pharmacology & microbiology at Surat. Hence the present study explores the emergence of sensitivity and resistance of most commonly used Cephalosporins.

2. Materials and Methods

This prospective study was conducted in the department of Pharmacology & Microbiology at Surat. Indoor and outdoor patient's samples such as pus, urine sputum, blood, endotracheal secretion, catheter tip and semen as sent by respected clinical department were collected. These samples were under gone to culture and sensitivity test. The study was conducted for a period of 12 months from March 2014 to April 2015. 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) [9]. 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 ºC 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 [10].

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) Cefipeme 50µg / disc
(9) Cefuroxime 30µg / disc

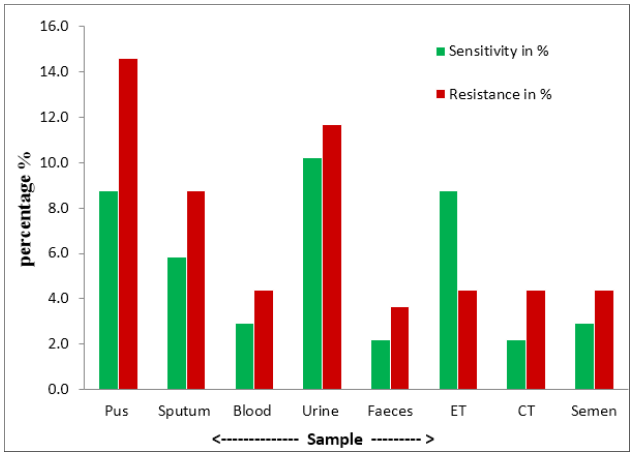

Fig 1: Percentages of samples collected. (n=685)

3. Result

A total of 685 clinical samples were collected, out of them 23.4% are pus, 14.6% sputum, 7.3% blood, 21.9% urine, faeces 5.8%, 13.1% endotracheal tube, 6.6% catheter tip and 2.9% of semen samples. Among the 160 Pus samples that are collected, 100 samples have shown resistance, and the remaining has shown sensitivity; Among the 100 Sputum samples collected, 60 samples have shown resistance, where the remaining has shown sensitivity; Among the 50 Blood samples collected, 30 samples have shown resistance, and the remaining samples has shown sensitivity; Among the 150 Urine samples collected, 80 samples have shown resistance, and the remaining has shown sensitivity, Among the 40 Faeces samples collected, 25 samples have shown resistance, and the remaining has shown sensitivity, Among the 90 Endotracheal samples collected, 30 samples have shown resistance, and the remaining has shown sensitivity, Among the 45 catheter tip samples collected, 30

Samples have shown resistance, and the remaining has shown sensitivity and among the 50 Semen samples collected, 30 samples have shown resistance, and the remaining has shown sensitivity.

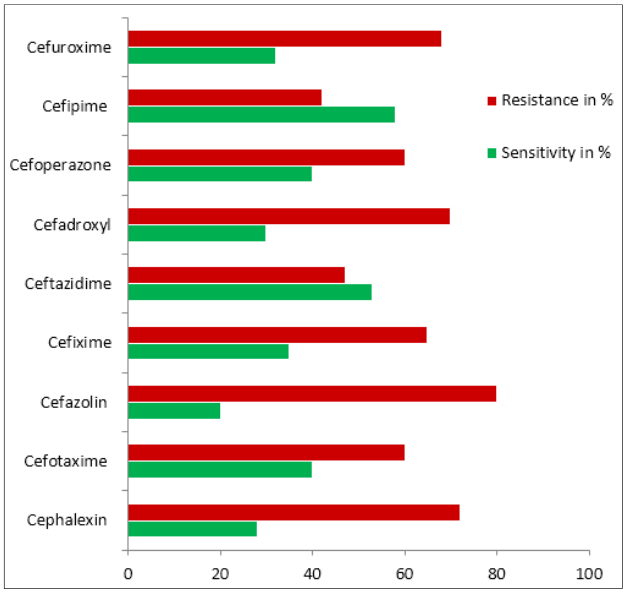

Fig 2: Sensitivity and resistivity pattern of Cephalosporins in percentages. (n=685)

4. Discussion

In the present study on Sensitivity of Cephalosporins, as per the above graph, First generation Cephalosporin drugs like (*Cephalexin, cefazolin, and Cefadroxil*) 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 in the third generation drugs like *Cefotaxime, Cefixime, Cefoperazone* has shown more resistance, than sensitivity whereas *Ceftazidime and* fourth generation drugshas shown sensitivity. 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 [11, 13]. 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 [14]. Various microorganisms of gram positive organisms like Staphylococci aureus and Staphylococci epidermis, Staphylococcus pneumoniae, Streptococcus pyogenes and gram negative organisms like Klebsiella, Pneumoniae, E. colli, Shigella and other organisms like Haemophilus influenza, Enterobacteria, 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, osteomyelitis, 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 685 samples with blood, urine, pus, sputum, endotracheal, catheter tip and semen were collected which consists of pus 23.4%, sputum 14.6%, blood 7.3%, urine 21.9%, faeces 5.8%, endotracheal 13.%, catheter 6.6%, semen 7.3% and among the 160 Pus samples that are collected, 100 samples have shown resistance, and the remaining has shown sensitivity; among the 100 Sputum samples collected, 60 samples have shown resistance, where the remaining has shown sensitivity; among the 50 Blood samples collected, 30 samples have shown resistance, and the remaining samples has shown sensitivity; among the 150 Urine samples collected, 80 samples have shown resistance, and the remaining has shown sensitivity, among the 40 Faeces samples collected, 25 samples have shown resistance, and the remaining has shown sensitivity, among the 90 endotracheal samples collected, 30 samples have shown resistance, and the remaining has shown sensitivity, among the 45 catheter tip samples collected, 30 samples have shown resistance, and the remaining has shown sensitivity and among the 50 Semen samples collected, 30 samples have shown resistance, and the remaining has shown sensitivity. The total 685 samples, Cephalexin shown 28% sensitivity and 72% resistance, Cefotaxime shown 40% sensitivity and 60% resistance, Cefazolin shown 20% sensitivity and 80% resistance, Cefixime shown 35% resistance and 65% resistance, Ceftazidime shown 53% sensitivity and 47% resistance, Cefadroxil shown 30% sensitivity and 70% resistance, Cefoperazone shown 40% sensitivity and 60% resistance, Cefipime shown 58% sensitivity and 42% resistance, Cefuroxime has shown 32% sensitivity and 68% of resistance. In a study, on in vitro 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 Cefoperazone have shown 89.8% sensitivity. But in our study, Ceftazidime have shown a considerably a significant sensitivity about 53% [15], and Cefoperazone have shown considerably a significant sensitivity about 40%. 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 (23.4%) 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 3rd generation cephalosporins like Ceftazidime, Cefotaxime Ceftriaxone. Where as in the present study Ceftazidime have shown 47% resistance, and Cefotaxime showed 60% resistance as compared to ceftazidime, whereas Cefazolin have shown 80% of resistance [16].

A Study conducted by A. Chaudhury in 2003 on in vitro activity of Cefpirome 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. 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 [17].

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 14.6% 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 3rd 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% [16]. 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 42%, was seen. Conclusion if the study is first generation Cephalosporin drugs like (*Cephalexin, cefazolin, and Cefadroxil*) has shown more resistance, than sensitivity, coming to the second generation drugs like *Cefuroxime and* third generation drugs like *Cefotaxime, Cefixime, Cefoperazone* has shown resistance more or less equal to first generation drugs, and the third generation drug like *ceftazidime* has shown mild sensitivity than fourth generation drugs like *Cefipime.*

5. Conclusion

Finally, the study concludes that the *ceftazidime* and fourth generation Cephalosporins have better sensitivity when compared to first, second and some third generation Cephalosporins. Here by, the present study explores the emergence of sensitivity and resistance of organisms to Cephalosporins in a tertiary care hospital.

6. Conflicts of Interests

Nil

7. Reference

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