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Antibiotics Surveillance Program: Survey on the Resistance Patterns of Microorganisms to Antibiotics in Nosocomial Infections.

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Research Article

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Abstract

The emergence of resistance to antimicrobial agents is a global public health problem, particularly in pathogens causing nosocomial infections. Antimicrobial resistance results in increased illness, deaths, and health-care costs. The study was carried out over a period of six months from July 2011 to January 2012. During the entire study period, a total of 69 patients antibiogram report were collected. Of these, 25 patients were identified as Nosocomial infections. Among these 25 patients, 64% (n=16) were male and 36% (n=9) were female. Age group analysis of the patients showed that, the most prominent age group were '61-70' years comprising of 32% (n=8). The study showed that the most important department generating the highest number of positive cultures were neurology department with 36% (n=9). Nosocomial infections contribute to extra hospital days and causing extra charges per hospitalization. During the entire study period showed that most of the patients received one antibiotic as per their treatment schedule i.e 52% (n=13), The most commonly prescribed antibiotics during the entire study period were Amoxicillin/ Clavulanic acid (21.88% prescriptions). Out of the 25 cases identified, gram-negative organisms were highly prevalent. This study conveys that the major reason for antibiotic resistance is the inappropriate use of antibiotics due to lack of uniform policies. So it is the time to think, plan and formulate a strong antibiotic policy to address this present scenario. Hence in the near future itself antibiotic prescribing guidelines have to be prepared and implemented for Nososcomial infections.

Keywords: *Prevalence, resistance pattern, microorganisms, infections, nosocomial*

Introduction

The emergence of resistance to antimicrobial agents is a global public health problem, particularly in pathogens causing nosocomial infections. Antimicrobial resistance results in increased illness, deaths, and health-care costs. The distribution of pathogens causing nosocomial infections, especially antimicrobial-resistant pathogens, changes with time and varies among hospitals and among different locations in the same hospital.[1]

The increasing number of immunocompromised patients and increased use of indwelling devices, as well as widespread use of antimicrobial agents in hospital settings, particularly in intensive care units (ICUs), contributes to antimicrobial resistance among pathogens causing nosocomial infections.

ANTIMICROBIAL RESISTANCE:

AMR is the expression of the ability of microbes to resist the actions of naturally occurring or synthetically produced compounds inimical to their survival. In a clinical context, AMR refers to a reduction in clinical efficacy so that either the benefits for the individual of treatment with an antimicrobial drug or the benefits to general public health are compromised. (WHO)[2]

CAUSE:

- Inadequate national commitment to a comprehensive and coordinated response, ill defined accountability and insufficient engagement of communities;
- Weak or absent surveillance and monitoring systems;
- Inadequate systems to ensure quality and uninterrupted supply of medicines
- Inappropriate and irrational use of medicines, including in animal husbandry:
- Poor infection prevention and control practices;

- Depleted arsenals of diagnostics, medicines and vaccines as well as insufficient research and development on new products.[3]

An important cause of increasing antibiotic resistance is the selection of resistant bacterial strains by mutation and transfer of mobile resistance genes as a result of excessive antibiotic prescribing by hospital doctors. Increasing antibiotic resistance also caused by transmission of resistant bacteria within hospitals by cross colonization of patients via the hands of health care staff and subsequent spread between hospitals by transfer of colonized patients.

The use of antimicrobial agents is a powerful selective force that promotes the emergence of resistant strains. Thereby, the growth of antimicrobial resistance led a signal to reduce unnecessary antibiotic use and to improve treatment protocols to maximize the lifespan of these drugs. To reduce antimicrobial resistance, multiple and often conflicting recommendations have been made, which includes reduction of all antimicrobial classes, increased use of prophylactic antimicrobials to reduce colonization, rotation of different antibiotic classes in a temporal sequence, and simultaneous use of different antimicrobials for different patients.

Strategies to control antibiotic resistance in hospitals include multidisciplinary cooperation in implementing local policies on use of antibiotics and infection control measures, timely detection and reporting of the antibiotic resistant strains, improved surveillance, and aggressive control of transmission of epidemic resistant bacteria.

MECHANISM:

The four main mechanisms by which microorganisms exhibit resistance to antimicrobials are:

1. Drug inactivation or modification: for example, enzymatic deactivation of *penicillin* G in some penicillin-resistant bacteria through the production of β-lactamases
2. Alteration of target site: for example, alteration of PBP—the binding target site of penicillins in MRSA and other penicillin-resistant bacteria
3. Alteration of metabolic pathway: for example, some sulfonamide-resistant bacteria do not require para-aminobenzoic acid (PABA), an important precursor for the synthesis of folic acid and nucleic acids in bacteria inhibited by sulfonamides, instead, like mammalian cells, they turn to using preformed folic acid.
4. Reduced drug accumulation: by decreasing drug permeability and/or increasing active efflux (pumping out) of the drugs across the cell surface.[4]

SOME FACTS ABOUT AMR:

About 440000 new cases of multidrug-resistant tuberculosis (MDR-TB) emerge annually, causing at least 150000 deaths. Extensively drug-resistant tuberculosis (XDR-TB) has been reported in 64 countries.

Resistance to earlier generation antimalarial medicines such as chloroquine and sulfadoxine-pyrimethamine is widespread in most malaria-endemic countries. Falciparum malaria parasites resistant to artemisinins are emerging in South-East Asia; infections show delayed clearance after the start of treatment (indicating resistance).

A high percentage of hospital-acquired infections are caused by highly resistant bacteria such as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci.

New resistance mechanisms, such as the beta-lactamase NDM-1, have emerged among several gram-negative bacilli. This can render powerful antibiotics, which are often the last defense against multi-resistant strains of bacteria, ineffective.[5]

"Antimicrobial Resistance" chosen as World health day (April 7th) 2011 theme by WHO[6]

The three key, inter-related elements of the Strategy to control AMR are:

- ***Surveillance:*** to monitor "how we are doing" and provide the data on resistant organisms, illness due to them and antimicrobial usage necessary to inform action;
- ***Prudent antimicrobial use*:** to reduce the pressure for resistance by reducing unnecessary and inappropriate exposure of micro-organisms to antimicrobial agents in clinical practice, veterinary practice, animal husbandry, agriculture and horticulture.
- ***Infection control:*** to reduce the spread of infection in general (and thus some of the need for antimicrobial agents) and of antimicrobial resistant micro-organisms in particular.

NOSOCOMIAL INFECTIONS:

An infection acquired in hospital by a patient who was admitted for a reason other than that infection. An infection occurring in a patient in a hospital or other health care facility in whom the infection was not present or incubating at the time of admission. This includes infections acquired in the hospital but appearing after discharge, and also occupational infections among staff of the facility.

Nosocomial infections are one of the occupational biohazards that affect the health of individuals with or without predisposing factors. These are the infections acquired during hospital stay, which are found in 5 to15% (two million cases are estimated annually) of hospitalized patients and can lead to complication in 25to 33% of those admitted in ICU.

The increasing incidence of hospital acquired infections caused by antibiotic resistant pathogens has led to an increase in morbidity and mortality. Studies conducted in hospitals in Delhi and Mumbai report figures as high as 30%. Even in most advanced countries like US, as per Centre for Disease Control estimate hospital admission due to infections acquired from hospital stays is about 4.5%. Resistance results from the interplay of microorganisms, patients and the hospital environment including antibiotic use and infection control practices.

Material and Method

The study was conducted in Kovai Medical Center and Hospital; a modernized 657 bedded multidisciplinary advanced super specialty hospital at Coimbatore. It is one of the largest hospitals in Coimbatore which excels in diverse specialized fields like Nephrology, Neurology, Cardiology, Pulmonology, Orthopedics, Oncology, Dermatology, Gynecology, Endocrinology, Pediatrics, General medicine, General surgery, ENT, Dentistry, Gastroenterology and Physical medicine and rehabilitation.

Study Design:
The study was designed to determine the susceptibility of isolates of microorganisms to antibiotics. The details of the bacterial strains isolated from any specimens of patients suffering from nosocomial infections were collected and studied. The study is a Prospective observational study.

Study Site:
The study was conducted at the Department of Microbiology in Kovai Medical Center and Hospital, a super specialty hospital in Coimbatore.

Study Period:
The study was conducted over a period of six months from July 2011 to January 2012.

Study Population:
A total of 25 subjects were included in the study.

Study Criteria:
Inclusion Criteria
✓ Patients with positive cultures after 48 hours of hospitalization.
✓ Patients for whom antibiotic sensitivity testing was performed.

Exclusion Criteria
✓ Out patients
✓ Patients receiving antibiotics without obtaining antibiogram report.
✓ Patients who present with positive blood culture at the time of hospitalization.

Study Protocol:
Topic Selection
Current levels of antibiotic resistance have reached critical levels with many epidemic clones of multiply resistant organisms such as *Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli* and *Klebsiella species* causing increased morbidity and mortality, particularly amongst the elderly and immuno-compromised. Urgent action is needed locally, nationally and internationally to contain this epidemic. Resistance surveillance is well established as an essential cornerstone of any attempts to understand and control resistance. Hence this study focuses on antibiotic surveillance program to assess the extent of the problem.

Literature Review
An extensive literature survey was done on, antimicrobial usage, antimicrobial resistance, challenges of antimicrobial resistance, strategies to minimize the spread of antimicrobial resistance, importance of antibiogram surveillance method etc. The literatures supporting the study were gathered from various journals like Clinical Infectious Diseases, British medical journal, Journal of antimicrobial chemotherapy etc. The articles from the journals were mainly collected with the help of SCIENCE DIRECT, IOWA DRUG INFORMATION SYSTEMS (IDIS), MEDLINE and from other Internet sources. Informations were also gathered from documents published by WHO.

Development of patient data entry form
A well-designed data entry form was used for collecting data for this study. Data collected included patient details, antibiotics prescribed and other drugs prescribed. For every subject in this study patient name, inpatient number, date of admission, age, sex, ward of admission and length of stay in the hospital were recorded. Details of antibiotic therapy such as name of the antibiotics, dose, route of administration, frequency of administration and duration of therapy and antibiogram report were recorded.

Consent from Ethics Committee:
The authorization for conducting this study in the hospital was obtained from the Chairman and approved by Ethics committee Kovai Medical Center Research and Educational Trust, Coimbatore on 17th September 2011.

❖ **Prospective Study**
In this phase of study the details of patients for whom antibiotic susceptibility testing was done for nosocomial infections were collected prospectively from the microbiology laboratory and patient files were obtained directly from the wards thereby

obtaining antibiogram report and other patient's details for a period of six months from July 2011 to January 2012.

Results

The study was carried out at Kovai Medical Center and Hospital over a period of six months from July 2011 to January 2012. A prospective observational study in which data pertaining to the time period between July 2011 to January 2012 were collected.
During the entire study period, a total of 69 patients antibiogram report were collected. Of these, 25 patients were identified as Nosocomial infections. However, only the 25 subjects whose antibiogram reports were available were included in this study. The data of 25 patients were collected as part of the prospective study. The results of the study are as follows:

Evaluation of the demographic data of the subjects revealed that among the 25 patients included in this study, 64% (n=16) were male while 36% (n=9) were female. Nosocomial infections was more common among men than among women.[34] This gender disparity in Nosocomial infections could be also due to patients those who were admitted in ICUs, mainly from road-traffic accidents and men were more prone to this.

Age group analysis of the patients showed that, the most prominent age group were '61-70' years and '31=40' years each comprising of 32% (n=8) and 20% (n=5) respectively. Our data showed that majority of Nosocomial infection cases were among patients over 60 years old. This might be due to decrease in the immunity in this age group.[35]
The study showed that the most important department generating the highest number of positive cultures were neurology department with 36% (n=9) followed by Orthopedics 20% (n=5). Among these departments, most of the patients were admitted in ICUs only, and those who were critically ill or immunocompromised requiring mechanical support and indwelling devices.[35]
Nosocomial infections contribute to extra hospital days and causing extra charges per hospitalization.[36] Our study also showed that from a total of 25 cases, most of the patients 24% (n=6) were admitted for more than 30 days followed by 16% (n=4) were 6-10 days. So these longer hospital stay could be a major reason for the emergence of organisms resistant to the antibiotic therapy.

The monitoring of the antibiotic therapy among the patients those who were admitted during the entire study period showed that most of the patients received one antibiotic as per their treatment schedule i.e 52% (n=13) followed by 40% (n=10) patients were on more than one antibiotics. The usage of multiple antibiotics in the hospital settings could thus be a major reason for the increase in antibiotic resistance.

The most commonly prescribed antibiotics during the entire study period were Amoxicillin/ Clavulanic acid which was accounted by 21.88% prescriptions, followed by Cefoperazone/ Sulbactam (15.63%), Colistin (15.63%) and Amikacin (12.5%) etc.

Out of the 25 cases identified, gram-negative organisms were highly prevalent of 96% (n=24) than gram-positive organisms of 4% (n=1). However many studies revealed that gram-positive organisms have over taken gram-negative species in terms of prevalence.[35,38,39,34] The culture reports also specified the microorganisms isolated from each specimen. This data indicated the prevalence of *Klebsiella species* and *Escherichia coli* to be the highest over all other organisms during the entire study period. Isolates of *Klebsiella species* were found to be 72% (n=18) of all specimens while *Escherichia coli* isolates were found to be 20% (n=5) specimens. Followed by *Staphylococcus* and *Pseudomonas species* accounted by 4% (n=1) each.

The antibiotic therapy given to each individual was reviewed against the corresponding antibiogram report and the following observations were made. Of the 25 cases, 24% (n=6) of subjects the antibiotics given empirically were found to be sensitive to the microorganism according to the antibiogram. In 48% (n=12) of the patients, the antibiotics given empirically were changed according to the antibiogram report. In 28% (n=7) of the patients, the antibiogram reports did not translate into any changes in the choice of antibiotics given. These inadequate administration of antimicrobial treatment may contribute antimicrobial resistance which would be an important determinant of patient outcome.[37]

Antibiotic susceptibility testing was done on these isolates to determine the susceptibility of the isolate to an array of antibiotics which would determine the extent of resistance or sensitivity of the organism to each antibiotic. The following antibiotics were included the study for susceptibility testing according to the antibiogram reports.

Colistin, Tigecyclin, Amoxicillin/ Clavulanic acid, Piperacillin/ Tazobactum, Cefoperazone/ Sulbactum, Ceftriaxone, Cefotaxime, Cefepime, Ciprofloxacin, Ofloxacin, Levofloxacin, Moxifloxacin, Amikacin, Doxycycline, Imipenem, Ertapenem, Meropenem, Vancomycin, Linezolid.

Of the 18 isolates of *Klebsiella species*, 100% resistance were found in Amoxicillin/Clavulanic acid, Ceftriaxone, Cefotaxime, Cefepime, Ciprofloxacin, Ofloxacine, Levofloxacine, Moxifloxacine, Doxycycline while 94.12% in Cefoperazone/Sulbactum, 93.75% in Piperacillin/Tazobactum, 72.22% in Amikacin, Ertapenem, Meropenem. Similarly 100% sensitivity were found in Colistin and Tigecyclin followed by 33.33% in Imipenem, followed by 27.78 in Meropenem and Ertapenem each.

All the 5 isolates of *Escherichia coli,* 100% resistant to Amoxicillin/Clavulanic acid, Ceftriaxone, Cefotaxime, Ciprofloxacin, Ofloxacin, Levofloxacin, Moxifloxacin, Doxycycline, Vancomycin, Linezolid while 80% resistant to Piperaciline/Tazobactum, Cefoperazone, Cefepime, Amikacin, Ertapenem and Meropenem, 60% for Imipenam. At the same time 100% sensitivity were found in Colistin and Tigecycline followed by 40% in Imipenam.

A total of 25 patients, 4% were identified as the isolates of *Staphylococcus aureus*. Of these, 100% resistance was found in Amoxicillin/Clavulanic acid, Piperacilline/Tazobactum, Cefoperazone/Sulbactum, Ceftriaxone, Cefotaxime and Cefepime. Similarly 100% of sensitivity was also found in Tigecycline, Doxycycline, Vancomycin. These observed results of Vancomycin also similar in the study carried out by Oteo et al.[17]

A total of 25 patients, 4% were identified as the isolates of *Pseudomonas* species. Among this 100% were found to be resistant to Amoxicillin/ Clavulanic acid, Piperacilline/Tazobactum, Cefoperazone, Ceftriaxone, Cefotaxime, Cefepime, Ciprofloxacine, Ofloxacine, Moxifloxacine and Doxycycline. At the same time 100% of sensitivity was also found in Colistin, Amikacin, Imipenem, Meropenem. The observed sensitivity to Imipenem is in contrast to the results given by Hanberger et al.[27]

Discussion and Conclusion

A total of 25 in-patients, included in the study between July 2011 to January 2012 and for whom antibiotic sensitivity testing was performed against various microorganisms isolated from their specimens, were reviewed during the entire study period. Nosocomial was more common among men than among women in this study. A high percentage of patients aged between '61-70' in this study population showed that patients over 60 years old are more prone to nosocomial infections.

The culture reports revealed that gram-negative organisms like *Klebsiella species, eshcerichia coli*, *pseudomonas species* were the predominant organisms causing HAI followed by *staphylococcus aureus*, a gram-positive organism. A total of 25 specimens containing 4 various microorganisms, underwent susceptibility testing against various antibiotics, among this 19 antibiotics were included in this study.

Combination of β-lactam antibiotics with β-lactamase inhibitors are now very commonly used in the treatment of various infections. It is usual for the physicians to use these combinations as empirical therapy. Among this group, Piperacillin/ Tazobactum and Cefoperazone/ Sulbactum were showed higher sensitivity than Amoxicillin/ Clavulanic acid against various microorganisms in this study. The result also showed that Piperacillin/ Tazobactum and Cefperazone/Sulbactum had essential sensitivity towards *Klebsiella species* and *Escherichia coli*.

During the entire study, Polymyxin antibiotics showed sensitivity to all microorganisms. Cephalosporins showed low sensitivity towards gram negative microorganisms. But Flouroquinolones showed fully resistant patterns in *Klebsiella species,E.coli, S.aureus* and *Pseudomonas.*

Amino glycoside (Amikacin) and Tetracyclin antibiotics are shown fairly good sensitivity towards all the gram-positive and gram-negative organisms involved in this study. Carbapenems like Imipenem and Ertapenem showed appreciable activity against gram-negative organisms in the entire study. Glycopeptide antibiotics such as Vancomycin and Teicoplanin showed appreciable sensitivity towards gram-positive organisms. However, since the sample size was inadequate, so the result could not be consider as accurate.

Furthermore, our data suggest that the most effective antibiotics remain for gram-positive organism such as *Staphylococcus aureus* in this study is Doxycyclin followed by Vancomycin and for gram-negative species such as *Klebsiella species, Escherichia coli, Pseudomonas aeruginosa* is Carbapenams followed by Piperacillin/Tazobactum.

The study emphasizes that, clinically significant Nosocomial infection is a serious consequence of a wide variety of initially localized infections, including those of the urinary tract, respiratory tract, surgical sites and indwelling devices such as central lines. Treatment is often urgent and may have to be undertaken without definitive identification of the organisms involved and their antimicrobial susceptibilities. These inadequate empirical therapy of nosocomial infections is associated with adverse outcomes, including increased mortality. Antimicrobial resistance is a common reason for these inadequate therapy. In this situation, knowledge of the most likely causative organisms and their expected resistance patterns can increase the probability of selecting an effective antimicrobial for empirical treatment. Timely surveillance studies can contribute reliable information to this knowledge base at national or regional level, although knowledge of local variations, at the level of individual hospital units etc.

Appropriate surveillance is also essential to monitor resistance trends and help to identify the factors that may be driving them. These surveillance systems make use of a network of laboratory-generated antibiograms that are constructed on the basis of the cumulative antimicrobial susceptibility data from each hospital. Antibiograms are currently used to estimate the impact of changes in antibiotic usage and to determine infection control strategies and antibiotic usage policies. Furthermore, antibiograms are often taken into account to define a rational selection of an empirical antimicrobial therapy for treating patients with hospital-acquired infections.

This study conveys that the major reason for antibiotic resistance is the inappropriate use of antibiotics due to lack of uniform policies and disregard for hospital infection control practices. So it is the time to think, plan and formulate a strong antibiotic policy to address this present scenario. Hence in the near future itself antibiotic prescribing guidelines have to be prepared and implemented for Nososcomial infections. Otherwise, empirical therapies will be ineffective which will in turn lead to widespread abuse of broad spectrum antibiotics which will ultimately result in further increase of resistance.

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AUTHORS' CONTRIBUTIONS

Authors contributed equally to all aspects of the study.

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests