Research Article

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Analysis of microbial resistance & prescription preferences using antibiograms

Abstract

Introduction: Hospital antibiogram is a periodic summary of antimicrobial susceptibilities of local bacterial isolates submitted to the hospital's clinical microbiology laboratory. It not only aids clinicians to select the most appropriate empiric therapy, but also in monitoring resistance trends within an institution, thereby optimizing treatment.

Aims: To analyze the susceptibility trends of microbes by using antibiograms; assess the modification in prescribing empirical therapy and examine application of the susceptibility report in clinical practice.

Settings and Design: A retrospective study of culture sensitivity reports and indoor prescriptions from departments of Medicine, Pulmonary medicine, Surgery, Orthopaedics, Obstetrics & Gynaecology & Intensive Care Unit.

Methods and Material: Culture sensitivity reports of samples collected from these specialties were analyzed for the susceptibility pattern of antibiotics. In addition, prescriptions were analysed for the prescribing patterns for antimicrobials.

Statistical analysis used: The data was tabulated using Microsoft Office Excel 2010 and were later compiled to make an antibiogram. Chi-square values were calculated using online software Graphpad Quickcalcs.

Results: After analysing the data it was found that the most common infecting organisms were Pseudomonas aeruginosa, Escherichia coli and Staphylococcus aureus susceptible to amikacin, piperacillin/tazobactam and linezolid. However the prescriptions analysed revealed that the commonly prescribed drugs were ceftriaxone and amoxycillin/clavulanic acid.

Conclusion: Antibiogram is useful in predicting and monitoring the trends of antimicrobial resistance. The survey revealed a clear mismatch between the sensitivity reports and the prescribing trends which can lead to evolution of multi-drug resistant organisms.

Key Message: To control development of antibiotic resistance institutions should have a multidisciplinary Drug and Therapeutic Committee in place to review and regulate antibiotic prescribing in order to ensure its appropriate use.

Keywords: drug and therapeutic committee, empiric therapy, susceptibility pattern

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Introduction

Discovery of antibiotics was one of the most celebrated achievements of modern medicine in 20th century. With the advent of 'Golden era of antibiotics', human life-expectancy has significantly increased by cure of previously fatal infections. However, almost half a century after introduction of these 'Wonder drugs', the emergence of stubborn, resistant microbes is the biggest threat we are facing right now. Antimicrobial resistance is defined as decrease in susceptibility of a microorganism to an antimicrobial agent to which it was previously sensitive. As a result, standard treatments become ineffective and infections persist and may transmit to others.[1] It's a matter of global concern since it possesses a significant clinical and financial burden. It is estimated that US$ 30 billion is spent on the cumulative effects of antimicrobial resistance each year including multiple drug regimens, extra hospital days, additional medical care and lost productivity. Studies show that mortality, duration of hospital stay and healthcare costs for patients with methicillin-resistant *Staphylococcus aureus* (MRSA) infections was higher as compared to methicillin sensitive S. aureus infections.[2]

Methicillin-resistant Staphylococcus aureus (MRSA) was first reported in 1961 and became endemic in many hospitals worldwide by 1980s. With the widespread emergence of MRSA, glycopeptide antibiotics such as vancomycin have been more frequently used in the clinical practice. This has led to sporadic cases of glycopeptides resistance. In the 90s, fluoroquinolone resistance in E.coli became prominent. The situation is still very volatile as infections caused by antimicrobial-resistant pathogen continue to haunt the clinicians. Furthermore, several highly resistant gram-negative bacteria-namely *Acinetobacter* species, multidrug-resistant (MDR) *P. Aeruginosa,* and carbapenem-resistant *Klebsiella* species and *Escherichia coli*, are emerging as significant pathogens in both the United States and other parts of the world. Our therapeutic options for these pan-antibiotic resistant micro-organisms are so extremely limited that clinicians are forced to re-introduce older, previously discarded drugs, such as colistin, that are associated with significant toxicity and for which there is a lack of robust data to guide selection of dosage regimen or duration of therapy.[3] To emphasize on their rising danger and the matter of fact that these pathogens conveniently 'escape' the effects of anti-bacterial agents, they were collectively termed ESKAPE group of organisms; where ESKAPE stands for Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumanii, Pseudomonas aeruginosa, and Enterobacter species.[4] Recently, Clostridium difficile too has been added to the list. Lately Indian subcontinent has been in the spotlight for Superbug containing the New Delhi metallo-β-lactamase 1 (NDM-1), an enzyme which makes the bacteria resistant to β-lactam antibiotics including Carbapenem group. So, it can be said that bacterial infections are becoming increasingly resistant to existing antibiotics, and, ironically, as the number of patients succumbing to these infections rise, the number of newer antimicrobial agents in the pipeline are dwindling.

One of the most important reasons for development of anti-microbial resistance is indiscriminate use of antibiotics. For example, antibiotics were prescribed in 68% cases of acute respiratory tract infections and of those, 80% were unnecessary according to CDC guidelines.[5] There may be many contributory factors to it like demands from patients, peer pressure, fancy perks from pharmaceutical industries leading to overuse of a particular type of antibiotic, diagnostic uncertainty, pressure to keep hospital-stay short and last but not least, physicians' lack of knowledge about the local susceptibility patterns which has been cited as one of the top causes. This is where cumulative antibiogram comes to the rescue.

Cumulative Antibiogram is defined as report generated by analysis of isolates from particular institution in a defined period of time that reflects percentage of 1st isolate per patient of given specie that is susceptible to each of antimicrobial agents routinely tested.[6] It is a pre-requisite for any antibiotic policy, to steer the physicians to select the most appropriate empiric antibiotic therapy. For instance, it is known that for patients in ICUs, mortality rises if the empiric antibiotic therapy chosen does not cover the pathogens causing the infection. Kollef et al.[7] showed that infection-related mortality was 17.7% in those patients who received appropriate empiric therapy and 42% in those who received inapt empiric antibiotic therapy.[7] The most common reason for the unsuitability of the chosen empiric antibiotic therapy was the resistance of bacteria to the antibiotic selected. In an effort to improve the adequacy of antibiotic selection, Ibrahim et al.[8] reviewed the antibiogram for their ICU and created a clinical guideline for antibiotic selection in that unit. The adequacy of empiric antibiotic selection for ventilator-associated pneumonia for patients in their ICU increased from 48.0% before the creation of antibiotic guidelines to 94.2% with the use of their guidelines.[8] Antibiograms are regarded as cost-effective and convenient method of assessment of local susceptibility rates and monitor resistance trends overtime in institutions.

The compilation and presentation of an antibiogram is generally initiated by the clinical microbiology laboratory with collaboration from clinicians, pharmacologists and infection control personnel. This document demonstrates recent, precise, and clinically useful data in an organized manner. The development of sophisticated computer programs like WHO-NET software and improvements in laboratory information systems assist in this process. The objective of our study was to analyze antimicrobial susceptibility trends by using Antibiograms and compare the susceptibility rates with the antibiotic prescribing patterns across the institution. This analysis was then used to orient the clinicians in attempt to rationalize their antibiotic prescribing habits and contain the emergence & spread of resistance.

Materials and methods

Study location

The present study was conducted in Guru Nanak Dev Hospital, Amritsar; adjoined to Government Medical College, Amritsar. It is a 1000 bedded tertiary care health institution. Departments included were Medicine, Pulmonary medicine, Surgery, Orthopedics, and Obstetrics & Gynecology.

Study period

For antibiogram preparation: From1st February, 2013to 31st July, 2013

Prescription analysis: From 1st May, 2013 to 31st July, 2013

Study Population: All the patients admitted to aforementioned departments during the period of the study were included.

Inclusion criteria:

a. Susceptibility reports of only Indoor patients were taken into consideration.

b. To prepare the antibiogram 1st diagnostic isolate of given specie per patient per analysis period was included, irrespective of body site, antimicrobial susceptibility profile or other phenotypic characters.[9]

c. Blood, urine and pus cultures were included.

d. Prescriptions of adult patients above 18 years with antibiotic medications were collected for analysis.

Exclusion criteria:

A. Antibiotic sensitivity test reports from laboratories other than Microbiology department of our institute were excluded

B. While preparing the antibiogram, the following isolates were excluded:

  i. Duplicate bacterial isolates

  ii. Surveillance culture and screening isolates

  iii. Isolates of the colonizers[10]

  iv. Strains which show intermediate susceptibility

  v. CSF isolates

C. Patients already on antibiotics were also excluded

The approval of the ethics committee of the institution was obtained

Citation: Kaur I. Analysis of microbial resistance & prescription preferences using antibiograms. *Pharm Pharmacol Int J.* 2016;4(7):502–508. DOI: 10.15406/ppij.2016.04.00104

Data collection and analysis

To prepare antibiogram

Culture sensitivity reports for the aforementioned departments were collected and since least no of culture sensitivity reports were from Pulmonary medicine (423) therefore, we evaluated 400 culture sensitivity reports from each department. Antibiograms were prepared by plotting the number of isolates of a particular micro-organism against the antibiotic to which they were found susceptible.

For prescription analysis

A. Prescriptions for antibiotic empiric therapy from each of the aforementioned departments were collected during the study duration specified previously and all the prescriptions satisfying the inclusion criteria were included in the study. (Table II). Prescriptions were analyzed for empirical antibiotic therapy received, which was compared with the sensitivity pattern in the antibiogram.

B. To construct the antibiograms& prepare the final results, Microsoft Office Excel 2010 software was used. Statistical analysis of antibiotic prescription against organism susceptibility was done by Chi-square test (χ^2). Chi-square values were calculated using online software Graphpad Quickcalcs.

Results

Data from 2000 Culture sensitivity reports was piled up to prepare antibiogram and 1587 Prescriptions were evaluated for prescribed drug against its organism susceptibility for particular antibiotic in percentage. Most common infecting organism isolated in samples from various departments.

Total number of prescriptions analyzed for various departments. Antibiotic prescription versus organism susceptibility, along with their χ^2-value is given in the form of bar graph. All χ^2-values were found to be significant at p<0.0001.

Antibiograms and organism susceptibility to antibiotic vs its prescription are shown in Figure (1A-5A) & (1B-5B) respectively. Culture reports from medicine department showed that the organism susceptibility was maximum to Amikacin-81%(325) followed by Nitrofurantoin-44%(176) and Gentamycin-37%(150) but among the most prescribed drugs were ceftriaxone-33%(114) and Ceftriaxone/Sulbactum-13%(45). In Pulmonary Medicine organisms were most susceptible to Amikacin-87%(347) & Piperacillin-40%(161) but Amoxicillin/Clauvulinic acid-65%(186); was frequently prescribed followed by ceftriaxone-42%(120) and Azithromycin-30% (86). Reports from surgery showed organism sensitivity to Amikacin-56%(225) followed by Piperacillin-30%(118) & Gentamycin-29%(116) & and the commonly prescribed drugs were Amikacin-74%(240) followed by Amoxycillin/Clauvulinic acid-50%(162) and Piperacillin/Tazobactum-48% (1). Cultures from Orthopedics showed the organism susceptiblity to Amikacin-60%(241) followed by Linezolid-27%(108) and Piperacillin-22%(91). Amikacin-90%(283) was the most commonly prescribed drug followed by Cefoperazone/Sulbactum-65%(205) and Ceftriaxone/Sulbactum-34%(107). Obstetrics &Gynecologyantibiogram showed highest sensitivity to Amikacin-84%(339) followed by Gentamycin-45%(181) & Linezolid-35%(141) and the most commonly prescribed drugs were Gentamycin-64%(201) followed by Cefotaxime/Sulbactum-45%(141).

Figure 1A

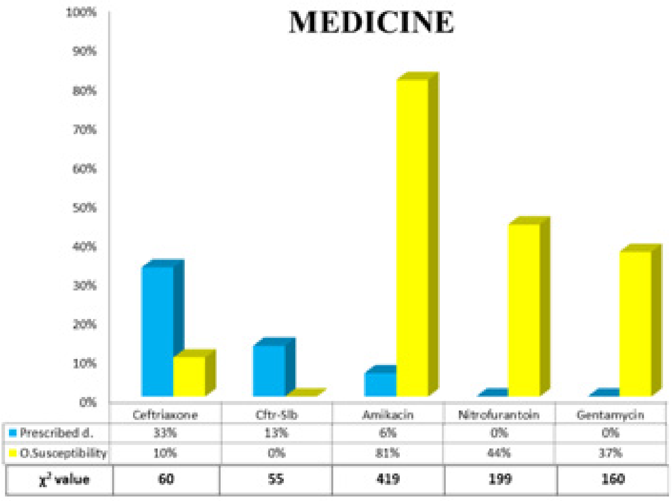

Figure 1B

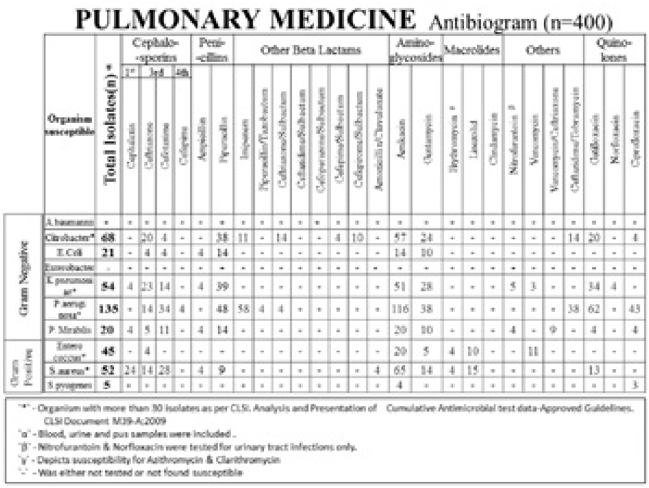

Figure 2A

Citation: Kaur I. Analysis of microbial resistance & prescription preferences using antibiograms. *Pharm Pharmacol Int J.* 2016;4(7):502–508.
DOI: 10.15406/ppij.2016.04.00104

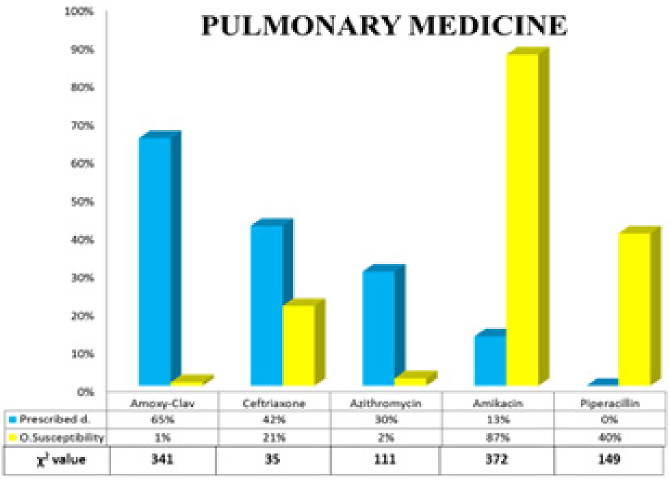

Figure 2B

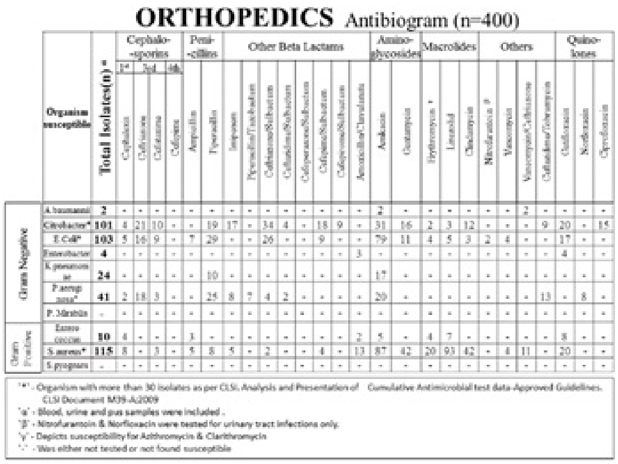

Figure 4A

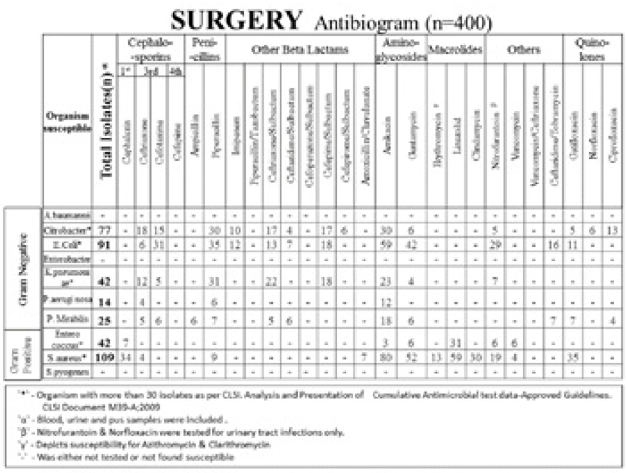

Figure 3A

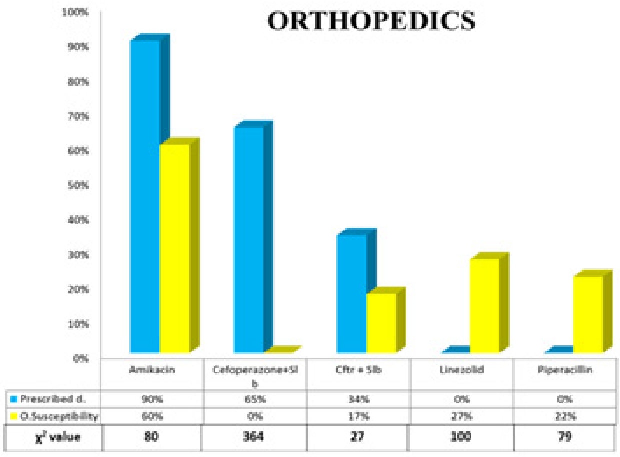

Figure 4B

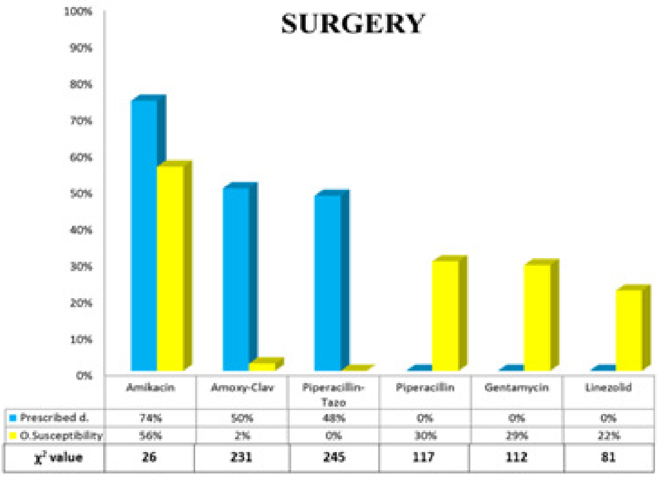

Figure 3B

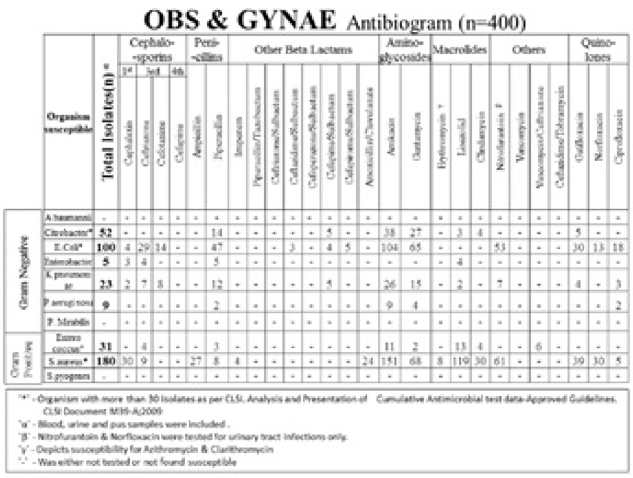

Figure 5A

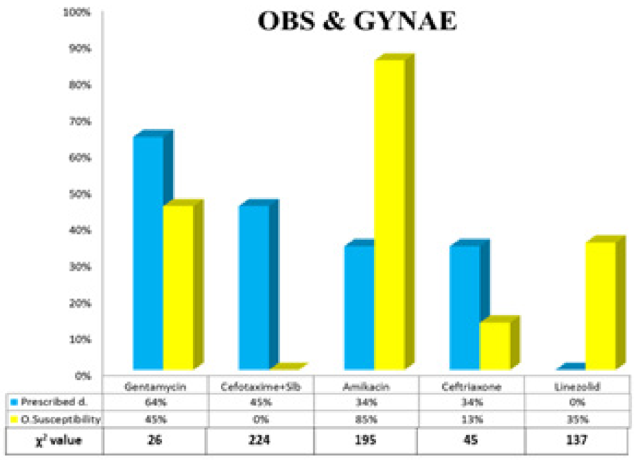

Figure 5B

Discussion

Antibiogram is a versatile document which, besides exhibiting the antibiotic susceptibility pattern across the institution, presents a clear picture of the most common disease-causing organisms in various units of the hospital. Nosocomial infections are a major public health concern these days and a cause of considerable mortality and morbidity for hospitalized patients. They occur among 7-12% of the hospitalized patients globally, with more than 1.4million people suffering from the infectious complications acquired in thehospital.[11]

Our study deals with the analysis of culture-sensitivity reports of only indoor patients, thus, the chances of coming across nosocomial or Hospital Acquired Infections (HAI) were high. In our study, the antibiograms of various departments indicated that most common pathogens isolated were gram negative bacilli [Medicine 72%, Pulmonary medicine 76%, Surgery 63%, Orthopedics 68% and Obstetrics & Gynecology 48%]. Among the array of gram negative organisms, the Enterobacteriaceae family was the most frequently identified group overall. Recent data from the U.S. National Healthcare Safety Network indicate that gram negative bacteria are accountable for more than 30% of hospital-acquired infections.[12] Among the HAIs caused by Gram negative bacilli, urinary tract infections were most prevalent. Klevens et al.,[13] have reported in their study that UTI accounts for more than 30% of infections reported by acute care hospitals.[13] Most of it has been found to be related with catheterization, generally known as Catheter-associated Urinary tract infection (CAUTI).Urinary catheters are used routinely in the wards of our hospital, usually for frequent and accurate monitoring of urinary output. And this can lead to increase in number of isolates of Gram negative pathogens.

In Pulmonary medicine ward, the most common individual organism was *Pseudomonas aeruginosa* (35%). This finding is in agreement with reports from USA which suggest that *P. aeruginosa* is the most frequent bacterium isolated from the respiratory tract (31.6%).[14] This can be attributed to patients of Community and Hospital-acquired pneumonia admitted in that ward. Hospital-acquired pneumonia by P aeruginosamay also be iatrogenic. Being an extremely adaptable organism it can survive and multiply even with minimal nutrients, if moisture is available. Thus, equipment such as respirator and bronchoscopes can be frequently contaminated.

On analysis of culture-sensitivity reports from Surgical units i.e. Surgery and Orthopedics, it was observed that Staphylococcus aureus (27% & 29% respectively) was most commonly encountered individual bacterial specie. This finding is supported by data from CDC which states that Staph. aureus is one of most prevalent organism associated with surgical wound infections.[15] This is also in accord with a study done by Kollef on surgical nosocomial infections which reported 31.1% isolates of Gram-positive bacteria.[16] Furthermore, S. aureus was the major pathogen from patients in Gynecology and Obstetrics wards (45%) and most commonly isolated bacteria from patients who underwent emergency type of surgery which may be due to surface contamination by this bacterium on the skin and environment causing nosocomial infections.

Antibiotics are one of the pillars of modern medicine and play a vital role both as the prophylaxis and management of infectious diseases. Successful treatment of patients with bacterial infection relies on the identification of bacterial pathogens and on the selection of an antibiotic effective against that particular organism. The issue of their availability, cautious selection and rational use are of critical importance to the global community.[17]

In the present study, on carefully comparing the prescriptions for empiric antibiotic therapy with the antibiograms, we observed that in Medicine, the most prescribed drugs were Ceftriaxone (33%), followed by Ceftriaxone-Sulbactam combination (13%) but the organism susceptibility of these antimicrobial agents were only 10% (χ^2= 60) and 1% (χ^2=55), respectively. On the other hand, Amikacin & Gentamycin showed a remarkable organism susceptibility, 77% and 36%, respectively, but these drugs were rarely prescribed [Amikacin=7% prescription rate (χ^2= 419) and Gentamycin = nil (χ^2= 160)]. Likewise, in Pulmonary Medicine, the antibiotics which were most frequently prescribed i.e. Amoxicillin-clavulanic acid (65%), Ceftriaxone (42%) and Azithromycin (30%), showed a very dismal [Amoxicillin-clavulanic acid = 3% (χ^2= 341)] or no [Ceftriaxone (χ^2= 35) & Azithromycin (χ^2= 111)] organism susceptibility at all. But, Amikacin, with exceptionally high organism susceptibility (86%), was uncommonly prescribed (χ^2= 372).

The Surgical branches demonstrated a healthier scenario regarding prescription of Aminoglycosides. In Surgery, Amikacin showed 57% organism susceptibility and was prescribed in 74% cases (χ^2= 26). In Orthopedics, Amikacin demonstrated highest organism susceptibility (58%) and was prescribed as an empiric therapy in 90% patients (χ^2= 80). In Obstetrics & Gynecology, even though, Amikacin displayed the highest organism susceptibility at 84%, Gentamycin, with 45% organism susceptibility, was the most prescribed antibiotic (64%, χ^2= 26) . However, the second most frequently prescribed antibiotics i.e. Amoxicillin-clavulanic acid (50%) in Surgery, Cefoperazone - Sulbactam combination (65%) in Orthopedics and Cefotaxim - Sulbactam combination (45%) in Obstetrics & Gynecology, showed very low or nil organism susceptibility. Thus, as evident by the χ^2 values (>200), there were greater discrepancies between second most prescribed antibiotics and organism susceptibilities.

Therefore to summarize, there was gross disparity between sensitivity pattern and the antibiotic prescribing trend in various wards. Irrational use of antimicrobials is the biggest contributing factor to the growing peril of resistance especially in low-income countries.[18] In our study, we observed a clear mismatch between culture-sensitivity pattern and antibiotic prescribing trend. Linezolid

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is a synthetic antimicrobial agent of the oxazolidinone class.[19] In this study, Linezolid illustrated an organism susceptibility rate of 23%, 27% and 38% in Surgery, Orthopedics and Obstetrics - Gynecology, respectively. However in all the three departments, it was not prescribed routinely. The most probable rationale behind this observation can be the fact that Linezolid is considered to be a 'Reserve Drug', set aside as an alternative agent for treatment of infections caused by multi-drug resistant strains like vancomycin-resistant E. faecium, nosocomial pneumonia caused by methicillin -resistant strains of S. aureus, complicated skin and skin-structure infections caused by MRSA.[20]

In the present study, antibiograms were segregated on the basis of different units where patients were admitted. Unit–specific antibiograms gives a superior picture of the organism susceptibility spectrum and thereby, the resistance trends since it is known that patterns of resistance to antibiotic vary widely between as well as within healthcare institutions.[21] In the same way, unit-wise antibiogram prepared in our study clearly depicted the variations in isolated micro-organisms, susceptibility trend and the antibiotic prescribing practices, as mentioned above. It also illustrated the odd resistance patterns in specific areas of the hospital. Institution-wide antibiogramsmay conceal important differences in susceptibility data across units within the institution. These differences may be significant, not only for selecting most effective empirical antimicrobial therapy for a patient in that unit but also for monitoring the emerging patterns of antimicrobial resistance specific to certain units within the institution.[22]

Limitations of the study & challenges of antibiogram

The present study had the following deficiencies:-

a) The antibiogram susceptibilities in our study may not forecast the best empiric drug combination because of unpredictable cross resistance. Cross-resistance should be taken into consideration to choose the initial combination regimens for serious gram negative infections, especially, P. aeruginosa[23].

b) Many culture sensitivity tests are frequently outsourced to the laboratories, other than our Institution's own Microbiology department. Hence, it is difficult to generalize the inferences of our findings for all the patients admitted.

c) Intensive care unit (ICU) was not included in our study since very few specimens were sent for culture sensitivity tests to the Microbiology department. It is because ICU is not an independent unit in our institution. The requests for culture sensitivity tests are sent by the respective departments under which the patient is admitted.

d) All the data was collected and analyzed manually. WHO NET software was not used.

Conclusion

The present study reveals a clear mismatch between susceptibility reports and prescribing trends which can give rise to antibiotic resistance. To rectify these discrepancies in prescribing pattern, Antibiotic policy and institutional Drug and Therapeutic Committee is one of the mandatory requirements for accreditation, and making an antibiogram is the first step before framing the antibiotic policy With a collaboration between departments of pharmacology, microbiology and the clinicians, it will not only review the antibiograms but will also regulate the antibiotic prescribing thereby enhancing its efficacy.

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Conflict of interest

Author declares that there is no conflict of interest.

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