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Standardizing Antimicrobial Prescribing Patterns and Emphasizing Microbiologist's Accountability: A Prospective Study

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ABSTRACT

Introduction:
Antimicrobial drugs are crucial to the therapeutic treatment of illnesses and are offered in both inpatient and outpatient settings. Most bacterial infections are treated with antimicrobials. Clinical treatment, the economy, and the environment are all impacted by their use. Using the wrong drug for an infection, delivering the wrong dosage, giving the right medication in the wrong way, and not completing the complete recommended course of treatment are all examples of antimicrobial misuse. The overuse and abuse of antibiotics leads to the development of antimicrobial resistance. Drug resistance has been observed in microbes of various kinds.
Hospital stays, mortality, morbidity, and medical costs are all increased by antibiotic resistance. Medical costs are higher for people with infections brought on by antimicrobial-resistant organisms than for those with illnesses brought on by organisms susceptible to antibiotics. Standardized prescribing procedures will result in more cost-effective health care. The study is to collect relevant clinical history, antibiotic prescribing patterns, and antibiotic sensitivity in addition to emphasizing the importance of a multidisciplinary approach in antimicrobial prescription.

Objectives:

1) To identify the clinical diagnosis and the antibiotics prescribed (either empirical or based on culture and sensitivity) for the patients enrolled in this study.
2) To identify the documented infective organism isolated and to identify the sensitivity / resistance patterns observed in these patients.

Methodology:
Every sample was processed by our microbiology department using pertinent clinical data gathered from the surgical and medical intensive care units. Both morphological and biochemical analyses were performed. On the same day, antibiotic sensitivity testing was performed in Mueller Hinton agar using 0.5 McFarland standards. Based on the size of the zone, the CLSI guidelines categorized the antimicrobials as susceptible, intermediate, resistant, dosage dependant, and sensitive. If any fungus was grown in Sabouraud's dextrose agar, then further processing was done based on the microscope's findings. All of the patient's information was collected from the doctors and case files, including the diagnosis, antibiotics given, dosage, duration of treatment, and length of stay. Costs, consumption rates, and the appropriateness of antibiotic use were all computed. Mortality rate was also calculated.

Conclusion:
The most frequently isolated organism in our investigation was Klebsiella pneumoniae, while the least frequently cultivated species were Streptococcus pneumonia and Enterococcus faecalis. Common specimens that commonly displayed microbial growth were urine, sputum, and pus. In half of the patients who tested positive for Staphylococcus aureus at first, an MRSA infection was later isolated from their urine and pus samples.

The most common clinical diseases for which antibiotics were recommended were lower respiratory tract infections, urinary tract infection-associated sepsis, and chronic obstructive pulmonary disease (COPD). There are a number of possible consequences when people are aware of the negative effects of antibiotic resistance, such as higher mortality, longer hospital stays, and higher expenses. Healthcare professionals can assist avoid such illnesses by using measures including infection-control strategies and antimicrobial agent management plans.

KEYWORDS: *Antimicrobial drugs, antimicrobial resistance, antimicrobial prescription*

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INTRODUCTION

Antimicrobial medications are provided in both inpatient and outpatient settings and are essential to the therapeutic management of diseases. Antimicrobials are the most commonly prescribed therapeutic agents and are crucial in the treatment of the majority of bacterial illnesses.(1) There are therapeutic, financial, and environmental ramifications to their use.

The morbidity and mortality from infectious diseases have been considerably decreased by antimicrobial medications. However, because of their inappropriate use, fast rising antibiotic resistance poses a threat to these gains. Antimicrobials used to treat viral or fungal infections or without evidence of infection are examples of inappropriate medication. Antimicrobial misuse is facilitated by prescribing the incorrect medication for an infection, giving the medication in the wrong dosage, or administering it in the wrong way, and not finishing the recommended entire course of treatment.

There have been reports of a high percentage of antibiotic prescriptions without bacteriological evidence or suspicion of a specific causative agent. Only when the physician is informed of the most likely infectious agents can rational prescribing be expected. Antimicrobial resistance develops as a result of the overuse and misuse of antibiotics. All types of microorganisms, including bacteria, viruses, fungi, and parasites, have developed drug resistance. Increased mortality and morbidity are being caused by an increase in multidrug-resistant life-threatening illness patterns.(2)

Ceftriaxone and metronidazole were the most commonly given antibiotics, while pneumonia was the most common infectious condition, according to a cross-sectional study conducted using World Health Organization (WHO) indicators.(3) The investigation revealed the absence of a hospital formulary or essential medicines list, a drug and therapeutic committee, and standard treatment guidelines for infectious diseases in the hospital. The outcome of the study revealed a high percentage of inappropriate antimicrobial and urged the need for multifaceted interventions and rational prescribing of antimicrobials.

Both patients and the medical community are aware of the prevalence of antibiotic resistance. The focus is on how antibiotic resistance affects clinical and financial results. It is generally known that the emergence of antibiotic resistance in *Staphylococcus aureus*, enterococci, and gram-negative bacilli is linked to higher rates of death, morbidity, duration of hospital stay, and medical expenses. Most patients' infections caused by antimicrobial-resistant organisms have poor outcomes due to inadequate or delayed therapy and significant underlying illness. Patients who have illnesses caused by organisms resistant to antibiotics incur higher costs than those who have infections caused by organisms responsive to antibiotics. In order to stop nosocomial emergence and the spread of organisms resistant to antibiotics, a multidisciplinary action plan is necessary.(4)

Since infections are the primary cause of hospital visits, antimicrobials have a substantial impact on health care expenses.(3) The emergence of antibiotic resistance raises hospital stays, mortality, morbidity, and medical expenses. Health care expenses are higher for patients with illnesses caused by organisms resistant to antibiotics than for those with infections caused by organisms responsive to antibiotics.(4) Standardizing prescription practices will reduce the cost of healthcare. In addition to highlighting the value of a multidisciplinary approach in antimicrobial prescription, the study aims to gather pertinent clinical history, antibiotic prescribing patterns, and antibiotic sensitivity.

Neonatal sepsis and neonatal hyperbilirubinaemia were the frequently encountered emergencies necessitating admission in neonates. Acute gastroenteritis and lower respiratory tract infections were the common causes for admissions in the older age groups. Baseline data on prescribing patterns among paediatric inpatients were studied by Shankar PR *et al.*,.(5) Apart from demographics, illness details, drug prescribing patterns, mean number of drugs prescribed per admission, the percentage of drugs prescribed from the essential drug lists, details of culture and sensitivity testing, the organisms isolated and their antibiotic sensitivity patterns, the mean cost of drugs per hospital admission and the percentage of the cost incurred on parenteral preparations and antibiotics were studied. Based on their observations, the following strategies were suggestions. Prescription by generic name, use of route conversion programs, reduction of antibiotic usage for viral infections and formulation of treatment guidelines for common conditions.

Sartaj Hussain *et al*., carried out a cross-sectional study to assess drug prescribing pattern at a tertiary care teaching medical institute.(6) One thousand prescriptions were randomly collected and analyzed using the world health organization prescribing indicators. The average number of drugs per prescription was 2.91. The percentage of drugs prescribed by generic name, from the essential drug list (National) and as fixed dose combinations (FDCs) was 10.05%, 22.57%, and 49.22%, respectively. The total percentage of encounters with antibiotics, injectables, and FDCs was 19.70%, 2.20%, and 73.60% respectively. The most common group of drug prescribed was gastrointestinal tract drugs (26.38%) followed by Vitamins and Minerals (23.12%), cardiovascular system drugs (11.56%) and antimicrobials (9.63%). They observed that the prescribing practices were inappropriate due to polypharmacy, lesser prescription by generic name and over prescription of FDCs. The need for improvement in the standards of prescribing patterns in many aspects was emphasized.

Supervision, audit and feedback accounts for the sequence of the action plan in promoting rational drug use. Appropriateness of the drug prescription should be audited. Evaluation of drug usage patterns with WHO drug use indicators is mandatory for promoting rational use of drugs. It is essential to find out and describe the various irrational ways of drug usage. In a prospective cross-sectional study done by Binaya Shrestha the prescribing trends in their hospital were analyzed.(7) Their study revealed polypharmacy and prescription writing using brand names to be the common irrational practices followed. They suggested prescription writings in generic name and the need for the development of antibiotics prescribing guidelines.

Objectives:

1. To identify the clinical diagnosis and the antibiotics prescribed (either empirical or based on culture and sensitivity) for the patients enrolled in this study.
2. To identify the documented infective organism isolated and to identify the sensitivity / resistance patterns observed

in these patients.

METHODOLOGY

Type of study: Descriptive study
Study design: Cross sectional study
Study population: The study involved patients admitted to the Medical and Surgical Intensive Care Units.
Study setting: Microbiology Department, Tertiary Care Hospital
Study period: 2 months
Sample size:A sample size of about 50 inpatients with clinically diagnosed infections in the Medical and Surgical Intensive Care Units were studied.

Selection Criteria

Inclusion criteria: Patients admitted to the Medical and Surgical ICUs during the study period with appropriate clinical details, for whom at least one antimicrobial drug was prescribed, were included in the study.
Exclusion criteria: Patients who were prescribed only topical antimicrobials and patients who dropped out during follow-up were excluded from the study.

Sample Collection and Processing

All samples received from the Medical and Surgical ICUs with appropriate clinical details were processed in the Microbiology Department. Direct smears were performed from all samples. Based on the Gram stain reports, clinicians were consulted regarding the initiation of empirical antibiotic treatment. Samples were plated on the following media and incubated for 24 hours:

- Blood agar
- MacConkey agar
- Chocolate agar
- CLED agar
- Brain Heart Infusion agar
- Sabouraud's Dextrose agar

Clinically relevant bacterial colonies were further analyzed using biochemical tests.
Biochemical tests for Gram-positive organisms: Catalase, coagulase, CAMP test, and bile esculin test.
Biochemical tests for Gram-negative organisms: Catalase, oxidase, motility test, indole, methyl red, Voges–Proskauer, urease, citrate, triple sugar iron agar, mannitol motility test, sugar fermentation tests, LAO decarboxylation test, and nitrate reduction test.
Species identification was done based on the biochemical reactions.
Antibiotic sensitivity testing was performed on Mueller–Hinton agar using 0.5 McFarland standards. Based on zone sizes, antimicrobials were classified as **sensitive**, **susceptible dose-dependent**, **intermediate**, or **resistant**, according to CLSI guidelines. E-strip testing was also performed. If fungal growth was observed on Sabouraud's Dextrose Agar, further processing was based on microscopy results. All patient details were collected from clinicians and case sheets, including diagnosis, antibiotics prescribed, dosage, duration of treatment, and duration of hospital stay. Appropriateness of antibiotic use, consumption rates, costs, and mortality rate were calculated.
Proposed intervention (if applicable): No interventions were done for the patients for sample collection.

Data Analysis

Antimicrobial prescription was assessed based on:

- Type of use
- Site of infection
- Route of administration
- Antimicrobial agent used
- Dosage
- Frequency
- Duration of treatment

Based on type of use, prescriptions were classified as **prophylactic** or **therapeutic**. Therapeutic use was further classified as:

- Empirical (based on local epidemiological data), or
- Targeted (based on bacteriologically proven pathogen)

The study aimed:

1) To identify susceptibility of infections to antimicrobial agents and the development of drug resistance.
2) To assess the association between drug resistance and adverse outcomes (mortality, length of hospital stay, cost). (4,5,6)
3) To calculate the median number of hospital days and the cost of antimicrobials during hospitalization.

Based on the collected data, WHO prescribing indicators were evaluated:

- Average number of drugs prescribed per patient encounter
- Percentage of encounters with an antimicrobial prescribed
- Percentage of antimicrobials prescribed by generic name

- Percentage of antimicrobials prescribed from essential drug list/formulary (2,6)

Appropriate statistical analysis was performed. Data were entered in Excel and analyzed using **SPSS 2023** under statistician guidance.

Confidentiality

Patient confidentiality was maintained throughout the study period.

Ethical Consideration

The study was conducted only after obtaining prior approval from the **Scientific Research Committee and Institutional Ethics Committee** of the institution (**Ref. no.: 132/SVMCH/IEC-Cert/October23, dated 13/10/2023**). This study was performed in the Microbiology Laboratory. The clinical samples underwent standard microbiological analysis.

OBSERVATION AND RESULTS

A total of 50 samples that came to our laboratory fulfilling the selection criteria were analyzed. The spectrum of organisms that were isolated from the samples include *Acinetobacter baumanii* (4%) from the drain tips, *Enterococcus faecalis* (2%) and *E . faecium* (4%) in the urine, *Proteus mirabilis* (4%) in the pus, *Morganella spp* (4%) in the pus, *Klebsiella pneumonia* from the pus (8%), sputum (10%), urine (2%) and the throat swab (4%), *Candida albicans* in the pus (2%) and in the sputum (2%), Non albicans candida in the sputum (2%) and in the vaginal swab (2%), *Pseudomonas aeruginosa* in the pus (6%), drain tip (2%) and in the sputum (8%), *Staphylococcus aureus* in the pus (10%) and in the urine (4%), *Escherichia coli* in the pus (4%), sputum (2%), urine (10%) and the ear swab (2%) and *Streptococcus pneumonia* in the pus (2%). Refer Table 1.
Acinetobacter isolates demonstrated resistance for piperacillin-tazobactam, amikacin and ciprofloxacin. Enterococcus showed resistance to high level gentamicin, vancomycin, linezolid and ampicillin. *Escherichia coli* showed resistant to amikacin, ciprofloxacin, amoxicillin, cefazolin and nitrofurantoin. *Klebsiella pneumonia* showed resistance to piptaz, cefipime, meropenem, amikacin, ciprofloxacin, amoxicillin, cefazolin and nitrofurantoin. Morganella species revealed resistance to amikacin, amoxicillin and ciprofloxacin. *Proteus mirabilis* was resistant to piptaz, cefipime, tobramycin, amikacin, cefazolin and cefaperazone-sulbactam. *Staphylococcus aureus* showed resistance to ciprofloxacin, clindamycin, erythromycin and cotrimoxazole. Pseudomonas demonstrated resistance to cefipime, tobramycin, ciprofloxacin and amoxicillin. All the above organisms showed intermediate sensitivity to other antimicrobials. Multidrug resistant organisms were isolated from few organisms, mostly with acinetobacter, pseudomonas and *E. coli*. Methicillin-resistant *Staphylococcus aureus* was grown in few patients.

A clinical diagnosis helps clinicians to foresee the causative pathogens that would most likely fit the prevailing clinical syndrome. This will help the clinicians in narrowing down to the most relevant antibiotic. Empirical antimicrobials were started by the clinicians based on the anticipated cause of the infections. Appropriate antibiotics were added and essential modifications on the empiric broad spectrum antibiotics depending on the culture and antimicrobial susceptibility reports were made. After the culture results, several patients' medication costs were eliminated by switching antibiotics. In cases of severe sepsis, the medication was prolonged for almost a week. Patients who experienced a ventilator-associated event (VAE) were given supportive antibiotic therapy in addition to medications based on reports of antibiotic sensitivity. In successive cultures, some people were resistant to a small number of medications, which led to the prescription of stronger antibiotics. Due to the protracted infection, these patients had to stay in the hospital longer, which increased their financial burden. Antibiotic resistance develops as a result of empirical antimicrobials being used inappropriately. The expenses of antibiotics and the length of hospital stays were increasing. For treatment, several patients spent over a month in the hospital. The risk of hospital-acquired illnesses is significantly increased by longer hospital stays. Mortality rate was higher in patients observed with MDR organisms, mainly in sepsis and VAE.

Table-1: Percentage of organisms seen in different patients' samples

Type of Sample

Organisms	Pus	Blood	Drain tip	Sputum	Ear swab	urine	TRS/TRA	Vaginal swab
Acinetobacter baumannii	-	-	4%	-	-	-	-	-
Candida albicans	2%	-	-	2%	-	-	-	-
Proteus mirabilis	4%	-	-	-	-	-	-	-
Klebsiella pneumoniae	8%	-	-	10%	-	2%	4%	-
Enterococcus faecalis	-	-	-	-	-	2%	-	-
Enterococcus faecium	-	-	-	-	-	4%	-	-
Morgenella spp.	4%	-	-	-	-	-	-	-
Non albicans candida	-	-	-	2%	-	-	-	2%
Pseudomonas aeruginosa	6%	-	2%	8%	-	-	-	-
Staphylococcus aureus	10%	-	-	-	-	4%	-	-
Streptococcus pneumonia	2%	-	-	-	-	-	-	-
Escherichia coli	4%	-	-	2%	2%	10%	-	-

DISCUSSION

Prescription pattern monitoring studies analyze the rational use of drugs in patients, i.e. receiving medications appropriate to their clinical needs, in doses that meet their individual requirements, for an adequate period and at the lowest cost to them and their community. This is complimented by the use of the WHO core indicators in helping to improve the drug prescribing patterns and thus promote its rational usage. The most frequently isolated organism in our investigation was Klebsiella pneumoniae, while the least frequently cultivated species were Streptococcus pneumonia and Enterococcus faecalis. Common specimens that commonly displayed microbial growth were urine, sputum, and pus. In half of the patients who tested positive for Staphylococcus aureus at first, an MRSA infection was later isolated from their urine and pus samples. The most frequently isolated pathogen from individuals with ventilator-associated events was Klebsiella pneumoniae. Five patients out of the 50 passed away from sepsis, and MDROs were isolated from those patients urinary tract infections, lower respiratory tract infections, and chronic obstructive pulmonary disease (COPD) associated sepsis were the most frequent clinical conditions for which antibiotic were prescribed. Often, patients were prescribed three or more empirical antibiotics at the same time, and the antibiotics were switched during the course of the clinical course depending on the results of the antimicrobial testing or if the clinical state did not improve. There are a number of possible ramifications when people are aware of the negative effects of antibiotic resistance, such as higher mortality, longer hospital stays, and higher expenses. Healthcare professionals can assist avoid such illnesses by using measures including infection-control strategies and antimicrobial agent management plans. The study's findings could help policymakers monitor and stop the spread of microbes resistant to antibiotics and help healthcare professionals use antimicrobial medicines wisely. It will aid in the creation of more advanced antibacterial treatments and agents. It is necessary to evaluate the rational prescribing skill of the clinicians periodically by conducting prescription audits.

CONCLUSION

Antimicrobial resistance is frequently encountered in our clinical setting and its implications are paramount. Formulation of a policy for hospital antibiotic use and educational program creating awareness for health care providers is required. Prevention and control of the spread of antibiotic resistant organisms requires strict adherence to infection control policies, integrating antimicrobial resistance strategies into institutional goals and development of an action plan in dealing with patients colonized with resistant organisms. Polypharmacy and higher rate of parenteral antibiotics prescription is a matter of concern. Rational use of parenteral antibiotics and early switchover to oral antibiotics will curtail the expenditure incurred.

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