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Comparative Analysis of Antibiotic Use and Resistance Patterns in Hospitalized Patients

Dr.S. Ramachandran[1*]

[1*] *Department of Pharmacology, GIET School of Pharmacy, India. E-mail: ramachandran@giet.ac.in*

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Abstract

One of the most important health issues facing the globe today is antibiotic resistance. Inappropriate antibiotic prescribing frequently results in antibiotic resistance, exorbitant medication costs, and an increased risk of side effects. Antibiotics totalling 13,677.42 were prescribed, primarily for medical and surgical prophylaxis. The most usually administered antibiotic was ceftriaxone, followed by metronidazole and cefuroxime, with significant variations across years and wards. Cephalosporin antibiotics were the most often given class of antibiotic (43.73%). In all wards, the monitoring group's use of antibiotics was high (59.69%). Finding the overall resistance percentage for each antibiotic class was the main goal. Classifying classes according to total resistance, tracking changes over time, evaluating pathogen- and region-specific influences, and determining correlations between resistances to various agents within a class were secondary goals. According to earlier research, broad-spectrum antibiotics are overprescribed in hospital and home care settings, accounting for 28–68% of incorrect antibiotic prescriptions.

Keywords: Antibiotics, Antimicrobial Resistance, Hospital, WHO.

1 INTRODUCTION

The first worldwide surveillance report on antibiotic resistance was published by the World Health Organisation (WHO) in 2014. This report revealed that in six WHO regions, hospital-acquired Klebsiella pneumoniae was resistant to third-generation cephalosporins and carbapenems at 50% or higher, Staphylococcus aureus was resistant to methicillin, and Escherichia coli was resistant to both of these antibiotics at 50% or higher. The same survey also found that multidrug-resistant (MDR) bacteria, particularly Klebsiella pneumoniae, account for 45% of mortality in Africa and Southeast Asia (Janto et al., 2022). As a result of the growing trend in resistance, patients experience treatment failure, considerable morbidity and death, higher annual out-of-pocket costs, and overall higher healthcare costs (Munteanu et al., 2021). According to estimates, bacterial antimicrobial resistance (AMR) caused 4.95 million fatalities in 2019 and 1.27 million deaths in 2019 (Behzadi et al., 2022). Antibiotic consumption is currently rising globally as a result of growing purchasing power, rising health insurance costs, and the prevalence of several infectious diseases (Alamer et al., 2023). In Bangladesh, there have also been reports of excessive use of antibiotics in outpatient settings, both via doctor prescriptions and

self-medication. Two approaches are required to solve this issue: first, stopping the spread of resistant microbes, and second, using antibiotics sparingly in medical settings (Bobir et al., 2024).

The most often prescribed medications in hospitals are antibiotics, and improper use of these medications fuels the rise in antimicrobial resistance (AMR), a worldwide issue (Mohandas et al., 2024). The use of antibiotics has grown historically, which has put selection pressure on bacteria that are vulnerable and increased AMR. One of the most important issues facing public health is antimicrobial resistance (Veera Boopathy et al., 2024). Although it can occasionally not be totally eliminated, it can be controlled (Saleem et al., 2020). Thus, efforts to lower antibiotic resistance by using antibiotics appropriately have garnered attention on a global scale. In addition to raising hospital stays and medical expenses, treatment failure raises the chance of contracting Clostridium difficile infections as a result of antibiotic abuse (Pauwels et al., 2021). Ineffective law enforcement, unethical drug promotion, a high patient volume, inadequate testing facilities, drug availability, a lack of knowledge about medications, and a failure to follow instructions can all lead to irrational prescriptions (Vijayakumar et al., 2019).

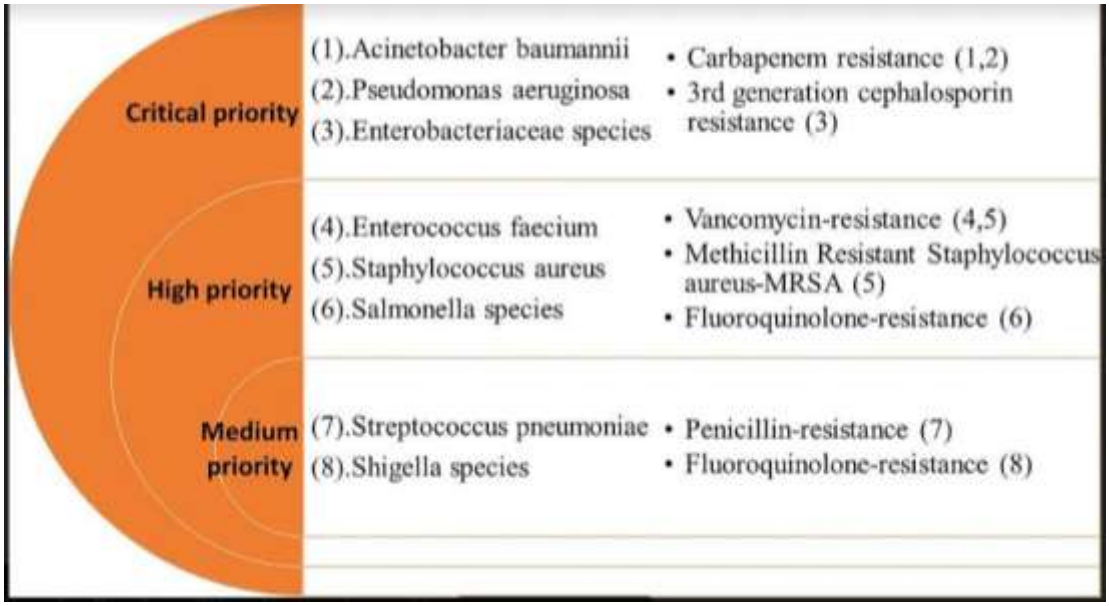


Figure 1: Based on the World Health Organization's Priority Pathogens list (WHO PPL), The Analysis Contained a List of Species and Antibiotic Resistance Patterns

Based on their resistance to certain medicines, twelve families of drug-resistant bacteria that are the biggest threat to human health have been divided into three priority categories: critical, high, and medium (Figure 1). In addition to calling for infection prevention and the prudent use of antibiotics in both humans and animals, this categorisation should place a high priority on and promote research and development of new antibiotics against particular drug resistance. It is well known that the world's population that uses antibiotics the most is Indian (Mugada et al., 2021). An action plan is thought to be necessary in order to tackle the AMR scenario, which presents major public health risks in India (Alamer et al., 2023). One of this action plan's five main initiatives is to use AMR surveillance to

strengthen the body of information and evidence. The antibiotic Resistance Surveillance and Research Network (AMRSN), which is centred on antibiotic resistance in six diseases in particular Indian hospitals, was founded by the Indian Council of Medical Research (ICMR) (Odeh & Taleb, 2023). 12 Outside of this network, not many Indian hospitals are monitoring AMR patterns in these diseases. Making educated judgements on AMR-related policies and practices in the area requires generating evidence related to AMR from a greater number of hospitals.

2 RELATED WORK

This NMA compares the resistance profiles of the main antibiotic classes used to treat troublesome Gram-negative bacteria using data from worldwide surveillance. Providing empirical advice for antibiotic selection is aided by class ranking determined by the sum of resistance rates. Regional antibiotic avoidance efforts and infection control programs may benefit from the identification of temporal and geographic trends. Information about how resistance spreads across organisms may be obtained through interactions between certain antibiotics (Vică et al., 2021). Clinical isolate susceptibility testing utilising EUCAST or CLSI breakpoints must be reported in included research. There are two steps involved in data extraction. The study quality is evaluated using the modified Newcastle-Ottawa scale. Using random-effects models, a network meta-analysis is carried out to produce a rating that assigns a resistance ranking to each antibiotic class. Subgroup and meta-regression studies are used to evaluate time trends, geographic differences, infections, and connections between individual antibiotics (Bogdan et al., 2021). NMA of antibacterial resistance data against significant Gram-negative bacteria for aminoglycosides, carbapenems, and fluoroquinolones. Every nation already has a public health system in place that places strict restrictions on the payment of unsuitable medications (Uyan, 2022). But all this technology does is look for differences between diagnosis codes and medications (Cesaro et al., 2023). Health officials have responded by implementing more creative criteria related to the use of antibiotics (Malathi et al., 2024). By cutting down on the time and amount of antibiotics administered, as well as by altering the scheduling of initial doses and using surgical prophylactic antibiotics, such initiatives should enhance the use of antibiotics both numerically and qualitatively.

PA genomes exhibit an amazing capacity to adjust quickly to changes in the environment, which promotes the quick development of adaptive genotypes and the subsequent creation of novel mechanisms for drug resistance. Mutations in the mucA gene have the potential to arise in non-mPAs, leading to an excess of alginate exopolysaccharide, which is an essential component of biofilms, and a shift towards a mucoid phenotype (Xing et al., 2024). A change in the virulence phenotype from an acute state, which is characterised by type III secretion, motility, and toxin production, to a chronic state, which is characterised by mucin secretion, biofilm formation, altered regulatory metabolic pathways, loss of quorum sensing (QS), and motility, occurs concurrently with this phenotypic transition from a non-mucoid to a mucoid state. Important acute virulence genes experience severe

adaptive loss-of-function mutations during this transition (Vittorakis et al., 2023). Expression of several virulence factors linked to both acute and chronic infections is dangerous to the host and should be taken very seriously, particularly in patients who are very sick and have a compromised mucosal barrier. This happens in some illnesses, like cystic fibrosis. Chronic obstructive pulmonary disease (COPD) and cystic fibrosis (CF) develop over decades, moving from sporadic colonisation to persistent infection.

In order to plan future antimicrobial stewardship initiatives and identify potential strategies and interventions for encouraging the prudent use of antibiotics, this study reviewed prescriptions for antibiotics using the WHO AWaRe categorisation.

3 MATERIAL AND METHODS

The Kirby-Bauer method was used to examine the antimicrobial susceptibility of a panel of antibiotic discs for both Gram-positive and Gram-negative pathogens. In short, Mueller-Hinton broth was used to generate a suspension of the test organism, the turbidity was adjusted to meet the McFarland 0.5 standard, and the mixture was incubated for two hours. Mueller-Hinton agar (MHA) plates were covered with antibiotic discs once bacterial lawns had grown on them. The plates were incubated at 370°C for 24 hours, and then the results were assessed for sensitivity, intermediate sensitivity, or resistance using criteria established by the Clinical Laboratory Standards Institute (CLSI). Measurements were also made of the zone of inhibition's diameter. A relational database system created especially for the study housed all of the patient data electronically. The data were then turned into tables for statistical analysis. The prevalence of antibiotic resistance was ascertained by calculating the percentage of positive results throughout the full study sample. SPSS 17 for Windows was used to conduct the statistical analysis. Z-tests for proportions were used to compare quantitative data that were reported as percentages. P values deemed significant were those that were less than 0.05.

3.1. Sample Data Collection

Demographic information (age and gender), duration of hospital stay, reason for hospitalisation, concurrent infections, invasive procedures (Foley catheter, nasogastric tube, mechanical ventilator, tracheostomy, arterial and venous catheter insertion, etc.), underlying diseases (diabetes, hypertension, etc.), organ function status (hypoalbuminemia, septic shock, liver dysfunction, renal failure, heart failure, respiratory failure, etc.), history of surgery within the previous year, steroid use history (within three months), levels of inflammatory biomarkers (within three days after evidence), use of antibiotics during hospitalisation, and efficacy of clinical clearance (effective, ineffective, unknown). By analysing the outcomes of bacterial reculture during hospitalisation, the bacterial clearance rate is calculated.

AR can worsen the prognosis of the illness, raise intolerance to AB therapy, and seriously impair the host immune system. Selective AB pressure on microorganisms is the common trend that unites all the components contributing to the multifactorial phenomenon that is the development of AR (Hillock

et al., 2021). Bacteria that carry or receive genes for AB AR are selected in a Darwinian manner because AB targets susceptible microorganisms. Bacteria containing AR genes are able to endure and grow in environments contaminated with AB (Rather & Mandal, 2023). The "horizontal gene transformation" process by which AR genes proliferate among other bacteria is known as "AR gene enrichment," which is facilitated by the uptake of mobile genetic components such integrons, plasmids, transposons, and gene cassettes as well as bare DNA material. It induces bacteriophages.

3.2. Patients and Method

AR was confirmed using the disk diffusion method. To differentiate bacteria, swabs and blood samples were cultured on MacConkey and blood agar plates and incubated at 37°C for 18–24 h. Identification of isolated microorganisms was performed by standard microbiological tests. All isolated strains were tested for antimicrobial susceptibility using the standard Kirby-Bauer disk diffusion test on Mueller-Hinton agar according to the guidelines of the Institute of Laboratory and Clinical Standards (Hall et al., 2022). Seven AB disks were used, namely azithromycin, amoxicillin-clavulanate, ceftriaxone, levofloxacin, gentamicin, meropenem, and vancomycin. All procedures performed in this study involving human body material were approved by the official ethical committee of the medical institution before conducting the study. Written informed consent was obtained from each participant prior to sample collection.

3.3. Susceptibility Testing

An automated Vitek-2 compact was used to identify the species of bacteria and determine their susceptibility to antibiotics (bioMerieux, France). Muir staining and the Congo red agar test were the two phenotypic techniques used to analyse the phenotyping of mPA and non-mPA isolates. On BHI agar containing Congo red and sucrose, non-mucoid strains generated pink to white colonies, whereas mucoid strains displayed red colonies (Odeh & Taleb, 2023). Specifically, PA ATCC 27853 was used as a quality control strain for the drug susceptibility testing of mPA, which was carried out using the Kirby-Bauer disc diffusion method and interpreted in accordance with the new CLSI M100 standard. WHONET 5.6 software was used to analyse the susceptibility test results (WHO, Geneva, Switzerland). The method of testing establishes if certain medications are susceptible to particular strains of bacteria. For instance, studies are conducted to determine how well aminoglycosides like tobramycin, gentamicin, and amikacin inhibit the target microorganisms (Eklöf et al., 2020). Penicillins like piperacillin and piperacillin-tazobactam, quinolones like ciprofloxacin and levofloxacin, cephalosporins like cefotetan, cefepime, and cefepimesulbactam, and carbapenems like imipenem and meropenem are also assessed for susceptibility. These assays aid in establishing the efficacy of these active components against the intended bacterium and in formulating suitable therapeutic plans.

3.4. Classification of Antibiotics

Beta-lactams, macrolides, glycopeptides, lincosamides, polymyxins, tetracyclines, fluoroquinolones, aminoglycosides, rifamycins, and azoles were the different categories of antibiotics. Other antibiotics for systemic usage include fosfomycin, which is administered orally. The beta-lactams that were examined included penicillins, combinations of beta-lactam/beta-lactamase inhibitor and cephalosporin/beta-lactamase inhibitor, as well as first-, second-, third-, and fourth-generation cephalosporins and carbapenems. A distribution analysis of antibiotics was conducted with the WHO AWaRe classification 2022.

The prevalence of multidrug-resistant bacteria has rapidly increased in the last several decades and is a major concern. There is an urgent need for methods to prevent bacterial resistance since the growth of resistant illnesses produced by these bacteria results in death and morbidity. The authors of this paper address a variety of strategies, such as the creation of novel antibiotic classes, combination treatments, natural antimicrobial compounds, and uses of nanoparticle systems, in addition to the mechanisms of antibiotic resistance, which include modifications in antimicrobial absorption and biofilm formation.

4 DISCUSSION

Over the course of the 5-year evaluation period, fewer individuals were admitted to hospitals, but the number receiving antibiotic treatment stayed mostly stable. Notably, the percentage of patients receiving antibiotics decreased slightly in 2020, while the number of patients receiving antibiotic treatment during the COVID-19 pandemic increased significantly in 2023 (Table 1) (Rusic et al., 2021).

Table 1: Number of Inpatients Treated with Antibiotics

	2019	**2020**	**2021**	**2022**	**2023**
Number of patients	41,598	26,138	27,755	41,598	39,743
Number of patients treated with antibiotics	22,928	21,182	13,135	15173	994,299

4.1. Antibiotic Utilization during Hospitalization

To analyse the correlation between PA antibiotic susceptibility test results and drug usage, and investigate antibiotic consumption differences between the two groups. Table 2 displays the utilization of antibiotics throughout the hospitalization period.

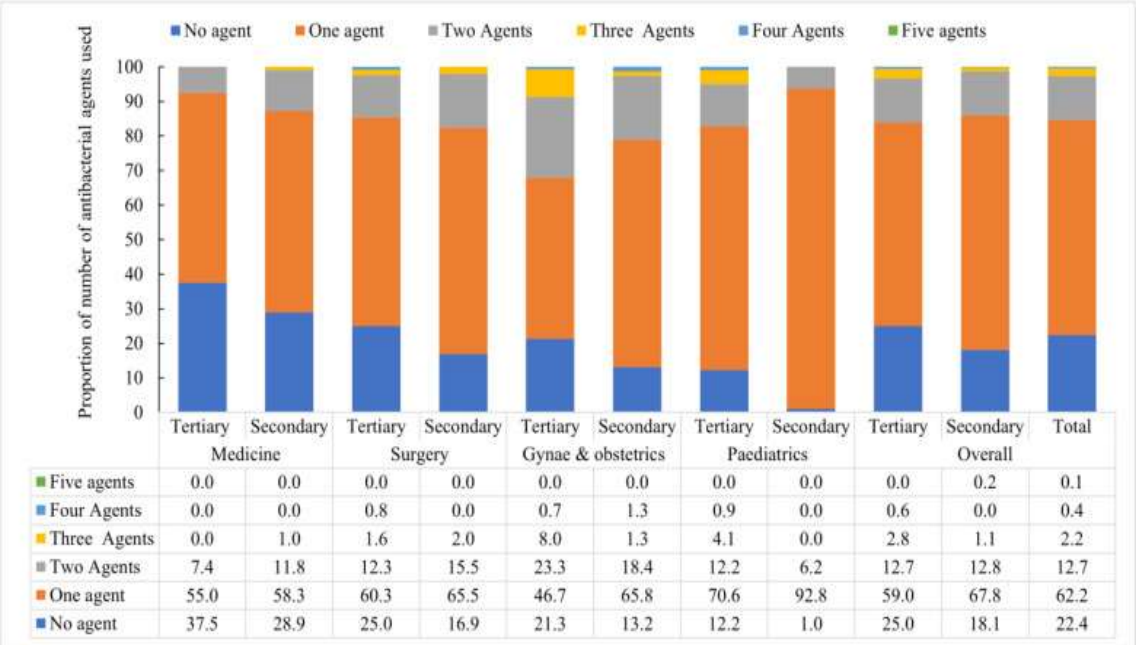
Table 2: Antibiotic Usage during Hospitalization in Patients with mPA and Non-mPA

Antibiotic	**mPA group (%)**	**non-mPA group (%)**	**p value**
Aminoglycosides	19(0.14)	76(0.09)	0.056
Quinolones	59(0.44)	382(0.45)	0.844
Penicillins	88(0.66)	607(0.71)	0.175
Cephalosporins	55(0.41)	467(0.55)	0.003
Carbapenems	29(0.22)	207(0.24)	0.495

In the present study, patients with mPA infection are predominantly female, with a more concentrated age distribution (Qin et al., 2022). Their hospitalization reasons are also more limited, primarily related to respiratory system diseases such as bronchiectasis and chronic obstructive pulmonary disease. On the other hand, non-mPA infection patients exhibit distinct characteristics. Their hospitalization reasons are primarily associated with cardiovascular and cerebrovascular diseases, and closely related to patients with diabetes ($p = 0.043$) and hypertension ($p < 0.001$).

4.2. Number of Antibiotics Used for Treating Patients after Admission

Between the time of admission and the survey date, 62.2% (882) of the 1417 registered patients received one antibiotic, or one antibacterial agent; 12.7% (180) received two antibiotics; 2.2% received three antibiotics (31); 0.4% (5) received four antibiotics; and 0.1% (1) received five antibiotics (Figure 2). In gynaecological and obstetric (28.3%; 64), surgical (15.7%; 63), and paediatric wards (13.8%; 44), there was a high rate of use of two or more antibiotics.



	Tertiary	Secondary	Tertiary	Secondary	Tertiary	Secondary	Tertiary	Secondary	Tertiary	Secondary	Total
	Medicine		Surgery		Gynae & obstetrics		Paediatrics		Overall		
Five agents	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.1
Four Agents	0.0	0.0	0.8	0.0	0.7	1.3	0.9	0.0	0.6	0.0	0.4
Three Agents	0.0	1.0	1.6	2.0	8.0	1.3	4.1	0.0	2.8	1.1	2.2
Two Agents	7.4	11.8	12.3	15.5	23.3	18.4	12.2	6.2	12.7	12.8	12.7
One agent	55.0	58.3	60.3	65.5	46.7	65.8	70.6	92.8	59.0	67.8	62.2
No agent	37.5	28.9	25.0	16.9	21.3	13.2	12.2	1.0	25.0	18.1	22.4

Figure 2: Number of Antibacterial Agents Used for Treating Patients During Hospitalization

5 CONCLUSION

High morbidity and mortality rates are linked to bacterial infections' antimicrobial resistance, which is a significant concern. Gram-positive and Gram-negative bacteria with multidrug resistance patterns are challenging to treat and could not respond to standard treatments. As a result of its unique capacity to adjust to the host environment, mPA displays comparatively mild clinical signs, as demonstrated by the results of our investigation. However, the extensive resistance to antibiotics exhibited by these strains frequently presents significant challenges in their eradication and results in patients experiencing chronic and permanent organ failure. Physicians may find it crucial to consider the variations in antibiotic resistance among distinct bacterial strains when choosing antibiotics in order to minimise

antibiotic abuse. Because of mPA's special capacity to stick together and form biofilms, lengthier treatment times and cautious preventive measures might be necessary. By helping doctors create proactive strategies and efficient clinical treatment regimens, these findings optimise clinical practice.

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