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Original Research Article

Evaluation of Current Practice of Antimicrobial Prescription in Patients with Bacterial Pneumonia at a Teaching Hospital: A Prospective Study.

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Abstract

Objectives: The primary intention of this study incorporated an analysis of the utilization pattern of antimicrobial drugs within the inpatients diagnosed with bacterial pneumonia (BP).

Material and Methods: A prospective observational study was undertaken within the Department of General Medicine to examine patients diagnosed with bacterial pneumonia (BP). Detailed records of antimicrobial prescriptions were precisely noted, with subsequent computation of both the Daily Defined Dose (DDD) and Antibiotics Consumption Index (ACI) in accordance with the World Health Organization Anatomical Therapeutic Chemical (WHO ATC) classification system. Additionally, adherence to WHO-prescribed indicators for antibacterial agent utilization was assessed. Dataset containing information of 130 patients was meticulously examined, and subsequent descriptive statistical analyses were applied employing Microsoft Excel and appropriate software packages.

Result: The predominant empirical therapy for antibacterial agents was found to be amoxicillin-clavulanic acid, utilized by 73 patients (56%), succeeded by levofloxacin, administered to 33 patients (25%). Following culture and sensitivity testing, the most frequently employed antibacterial agents for definitive therapy included levofloxacin for 31 patients (24.0%), ceftriaxone for 23 patients (17.7%), meropenem for 18 patients (13.8%), and azithromycin for 10 patients (7.7%) and Doxycycline for 6 patients (4.6%). Notably, the highest Antibiotics Consumption Index (ACI) value recorded was 14.2 for amoxicillin-clavulanic acid in empirical therapy, while for definitive therapy; levofloxacin exhibited an ACI of 14.6. A noticeable disparity in ACI values between empirical and definitive therapy was observed ($p<0.05$), suggesting statistically meaningful differences. Furthermore, a substantial proportion of patients, 115 individuals (88%), received multiple antibacterial prescriptions. The average number of drugs prescribed per patient was 7.69±2.2, with an average of 2.68±1.85 antibiotics per prescription. Approximately 34% of prescribed drugs were denoted by their generic names, indicating a notable size of generic drug usage within the study group.

Conclusion: The findings of the present study highlighted a significant pattern in the utilization of antibiotics for the treatment of bacterial pneumonia (BP) within the Medicine Department. This analysis focuses on the need for the implementation of antimicrobial treatment guidelines (Antibiotic policy) within the hospital setting, aiming to enhance the efficacy and rationality of antibiotic usage while concurrently optimizing the allocation of scanty healthcare resources. Such guidelines can work as a crucial framework for clinicians, promoting standardized practices and upholding judicious antibiotic prescribing practices, ultimately contributing to improved patient outcomes and minimisation of antimicrobial resistance. It can also be concluded that tertiary care hospital requires a coordinated mediation to improve rational use of antimicrobials and therefore the clinical outcomes also by improving efficacy and reducing the cost and the chances of adverse effects through establishing an antimicrobial stewardship program and strict implementation of Hospital Antibiotic policy.

Keywords: Antimicrobial agents, bacterial pneumonia (BP), Antimicrobial utilization pattern, Daily Define Dose (DDD).

Introduction

Bacterial pneumonia (BP) represents a substantial public health concern all around the world, posing a significant threat to individuals across diverse geographical and socioeconomic areas. BP a prevalent respiratory infection, is a significant medical concern, particularly among adult patients. This condition involves the lower respiratory tract, specifically targeting the bronchi, the prominent air passages responsible for air transport within the lungs. Acute pneumonia manifests as an inflammation of these bronchi without evidence of pneumonia and typically affects individuals without underlying chronic obstructive pulmonary disease (COPD) [1]. This infectious respiratory condition stands as a conspicuous cause of both hospitalization and mortality among adult populations, exerting its effect not only in developing nations but also in more economically advanced cultures. Mostly health care practioners and the patients frequently undermine the magnitude of bacterial pneumonia. The World Health Organization (WHO) advocates for the utilization of indicators to monitor trends in antibiotic usage, facilitating local agencies in pinpointing deficiencies and focal points for intervention. [2] The growing danger of antimicrobial resistance complicates BP therapy, as does the propensity to focus on empirical therapy. [3] Drug Utilization (DU) has emerged as a specific research domain, facilitating stringent examination of drug prescription and consumption patterns through systematic and formal methodologies. Such investigations illuminate the quality of drug prescribing practices, often assessed through predefined criteria such as the Defined Daily Dose (DDD). [4] The utilization of Defined Daily Dose (DDD) confers several advantages for objective evaluation, encompassing standardization, simplification, comparability, and trend analysis. This metric is instrumental in drug utilization studies, enabling the quantification and comparative assessment of medication usage across various therapeutic agents. [5]

This study holds promise for evaluating the prescription patterns of antibacterial agents utilized in the management of BP. Furthermore, our observations have illustrated a direct correlation between alterations in medication regimens and the progression of the disease. Such observations are invaluable for formulating guidelines tailored to the disease profile of BP with in a tertiary care hospital.

Material and Methods

The collaborative research was undertaken for duration of seven months and involved the Departments of Medicine and Pharmacology at a teaching hospital. Approval for the study was obtained from the Institutional Ethics Committee (IEC).

It was designed as an observational, prospective, and qualitative study on antibacterial drug utilization. Eligible participants were patients admitted to the internal medicine department with a diagnosis of bacterial pneumonia who were receiving antibacterial agents. They were enrolled and followed up from admission to discharge. Written informed consent was obtained from each participant upon enrolment. Patient records were collected at admission for empirical therapy, on the third day after medication change following sensitivity testing, and until they were finally discharged.

Inclusion Criteria: All patients of both sex and age above 18 years were included.

Exclusion Criteria

1. Patients already undergoing antimicrobial therapy for more than 7 days,
2. Patients with Ventilator-associated pneumonia,
3. Immunocompromised patients,
4. Patients diagnosed with Lung cancers, and
5. Individual with Tuberculosis

Out of a total 162 patients initially enrolled, 20 discontinued treatment prematurely, and 12 succumbed during the course of treatment. Therefore, prescription records of 130 patients were analysed over a six-month period.

Medication prescriptions were documented using the International Anatomical Therapeutic Chemical Classification Scheme (ATC). Consumption of antimicrobial agents was assessed utilizing the ATC-DDD classification system.

Unit of measurement Defined Daily Dose (DDD) [6]

The Defined Daily Dose (DDD) represents the standard average maintenance dosage of a medication utilized in adults for its primary indication. For drugs with an existing Anatomical Therapeutic Chemical (ATC) code, a specific DDD has been allocated.

$$\text{Number of DDDs} = \frac{\text{Total grams used}}{\text{DDD values in grams}}$$

DDD/bed-day x 100 = Antimicrobial consumption index (ACI). The number obtained is the hospital's antibiotic consumption index for BP. Quantifying antibiotic usage through the Antimicrobial Consumption Index (ACI) enables hospitals to compare their antibiotic consumption levels with those of other institutions, irrespective of variations in formulary composition, antibiotic potency, and hospital census. [7]

Statistical Analysis: The collected data was statistically analysed through SPSS version 27. Descriptive data were presented as percentages or the mean ± standard deviation.

Result

Patients included in the study belong to the 21–80-year age group. The mean age of individuals diagnosed with bacterial pneumonia was 64.65 ± 12.54 years. Among the patients presenting with bacterial pneumonia, majority were male, constituting 86 (66.1%), while approximately 44 (33.9%) were female shown in Fig. 1.

Antibacterial Agents Used as Empirical Therapy: The empirical therapy most commonly prescribed for antibacterial treatment consisted of amoxicillin-clavulanic acid, administered to 73 patients (56.1%), followed by levofloxacin for 33 patients (25.3%), ceftriaxone for 16 patients (12.1%), ofloxacin for 6 patients (4.6%), and piperacillin-tazobactam for 2 patients (1.5%).

Distribution of Antibacterial Agents as Definitive Therapy in BP: As definitive therapy, the most frequently utilized antibacterial agents included levofloxacin, prescribed for 33 patients (25.3%), followed by ceftriaxone for 25 patients (19.4%), meropenem for 18 patients (13.6%), azithromycin for 9 patients (6.8%), and vancomycin for 5 patients (3.7%). Less commonly used agents included linezolid, cefoperazone, and moxifloxacin, each administered to 1 patient (0.7%).

Antibacterial Dose Consumption: The highest Antibiotics Consumption Index (ACI) value observed for empirical therapy was 14.4, attributed to amoxicillin-clavulanic acid, followed by azithromycin with an ACI of 12.6. In contrast, for definitive therapy, levofloxacin exhibited the highest ACI of 14.6, followed by meropenem with an ACI of 13.1. A statistical comparison of empirical and definitive therapies regarding the antibiotics consumption index showed a p-value less than 0.05, indicating a statistically significant difference between the two therapies in terms of antibiotic consumption by patients. (Table-1)

Microbial Pathogens Isolated: Five pathogens were isolated via sputum culture, with Streptococcus pneumoniae being the most prevalent, affecting 48 patients (37%). Following this, Klebsiella pneumoniae was identified in 36 patients (29%), Escherichia coli in 31 patients (21%), Staphylococcus aureus in 10 patients (8%), and Pseudomonas in 5 patients (5%). (Fig-2)

Pattern of Combinational Antimicrobials Prescribed in BP Patients: In the management of Bacterial Pneumonia (BP), the most commonly prescribed combinations of antimicrobials were amoxicillin-clavulanic acid in conjunction with azithromycin, accounting for 43% of cases in empirical and 34.5% in definitive therapy. Conversely, the least frequently utilized combination was amoxicillin-clavulanic acid combined with amikacin, constituting only 3.1% of cases. Overall, multiple antimicrobial prescriptions were observed in 115 cases (88.4%). (Table-2)

Duration of Stay in Hospital: The hospital stay duration ranged from a minimum of 4 days to a maximum of 11 days, with a mean duration of 8.60 ± 1.48 days. The mean duration of empirical therapy was 4.01 ± 0.60 days, while that of definitive therapy was 5.57 ± 0.68 days.

Prescribing Indicators: The average number of drugs prescribed per prescription was 6.57 ± 2.17, with an average of 2.36 ± 1.67 antibiotics per prescription. Approximately 40% of drugs were prescribed using their generic names. On average, 90.4% of prescriptions included injections which amounted to around 117 patients.

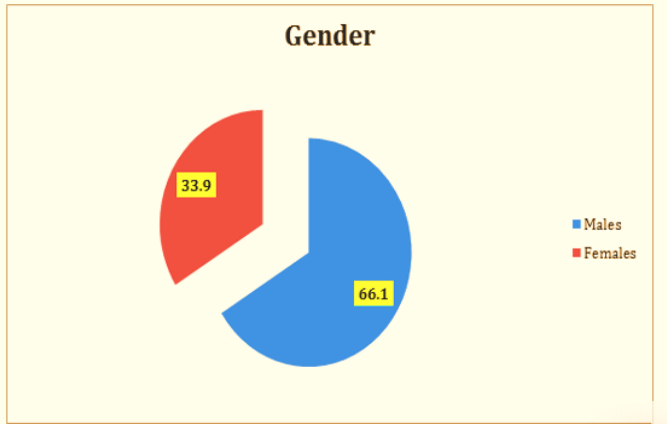

Figure 1: Gender distribution of Bacterial pneumonia patient

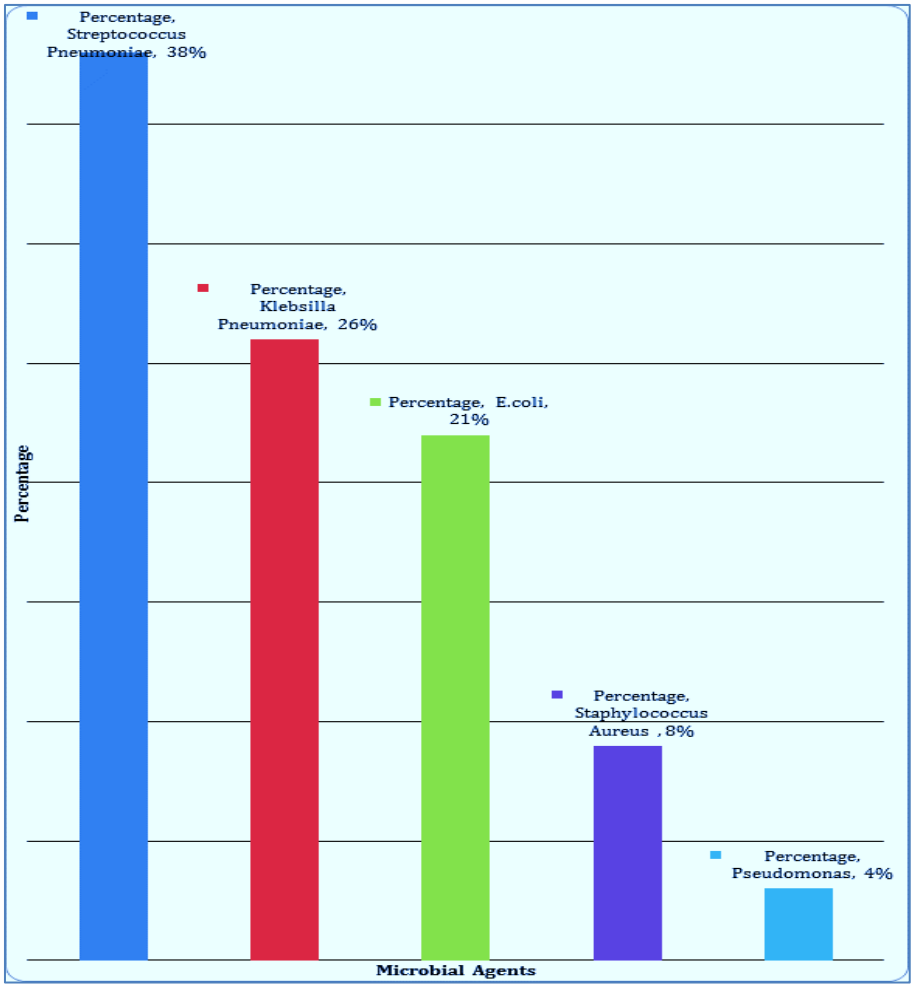

Figure 2: Percentage of microbial pathogen isolated in BP patients.

Table 1: Antibiotics Consumption Index (ACI) among empirical and definitive therapy of BP patients

Drug	DDD(gm.)	ACI=DDD/100 bed-days (empirical therapy)	ACI=DDD/100 bed-days (definitive therapy)
Penicillin –Amoxicillin-clavulanic acid (O)	1	14.2	5.52
Amoxicillin-clavulanic acid(P)	3	0.135	
Piperacillin-tazobactam	14		0.90
Cephalosporins			
Ceftriaxone	2	0.94	6.17
Cefoperazone	4		0.10
Macrolide			
Azithromycin (O)	0.3	12.6	5.14
Clarithromycin (O)	0.5		0.94
Fluoroquinolones			
Ofloxacin	0.4	0.62	1.6
Levofloxacin	0.5	6.47	14.6
Moxifloxacin	0.4		0.15
Tetracycline			
Doxycycline			0.18
Aminoglycoside			
Amikacin	1		0.83
Carbapenem			
Meropenem	2	0.18	13.1
Vancomycin	2		2.40
Linezolid	1.2		0.15

O= oral, P= Parental

Table 2: Frequency of combination antimicrobial prescription in BP patients

Antimicrobial agents	As empirical therapy n (%)	As definitive therapy n (%)
Amoxicillin-clavulanic acid+Azithromycin	43%	34.5%
Amoxicillin-clavulanic acid+ levofloxacin	18.2%	12.6%
Amoxicillin-clavulanic acid+ceftriaxone	4.36%	15.6%
Amoxicillin-clavulanic acid+ amikacin	0.5%	3.1%
Levofloxacin+azithromycin	13.5%	9.3%
Levofloxacin+ceftriaxone	12.4%	13.9%
Ceftriaxone+ azithromycin	6.9%	10.6%
Amoxicillin-clavulanic acid+ levofloxacin+ azithromycin	3.1%	2.8%
Total multiple prescriptions	57%	31.3%

Indicators of antimicrobials use:

Table 3: Indicators for prescription of antimicrobials

Indicators	Mean± S.D. / Percentage
Average number of drugs per prescription(encounter)	6.57±2.17
Average number of antibiotics per prescription	2.34±1.67
Percentage of drugs prescribed by generic name	40%
Average number of prescription with injection	117 (90.4%)

Discussion

Bacterial pneumonia stands out as one of the cause of hospital admissions among infectious diseases. Antimicrobial drugs form the basis of primary treatment approach, both empirically and upon confirmation of microbial pathogens by sensitivity testing. Nonetheless, their utilization has raised concerns due to instances of overuse and misuse, leading to occurrence of adverse drug events, significant emergence of drug resistance, extended hospital stays, and increased cost of treatments. This study seeks to outline the existing trends of antibacterial drug utilization in patients diagnosed with Bacterial pneumonia.

In this study, the highest proportion of cases (36.1%) fell within the age bracket of 55-70 years. The mean age of patients was recorded as 64.65 ± 12.54 years. Notably, approximately 67 cases were aged over 65 years.

Studies conducted by Menon *et al.* and Shah *et al.* have consistently demonstrated that the highest incidence of Bacterial Pneumonia occurs in patients aged over 60 years. [8,9] The extremes of age are associated with lower immunity and an increased prevalence of predisposing risk factors, which contribute to multi-organ failure. This susceptibility to multi-organ failure is often attributed to the predisposition associated with old age.

The predominant approach to treatment in Bacterial Pneumonia (BP) largely depends on observational methods, emphasizing clinical and radiological diagnoses of the most prevalent causative pathogens. However, BP remains a considerable public health concern. Therefore, it is crucial that antimicrobial treatment strategies be customized to align with the distribution and prevalence of etiological pathogens within the population. Resistance trends at the local, national, and international levels, alongside prior exposure, must all be carefully weighed in antimicrobial decision-making. Additionally, the decision regarding hospitalization is guided by prognostic criteria, ensuring optimal management of patients with Bacterial Pneumonia. The results of this study shows that amoxicillin-clavulanic acid along with azithromycin (43%) and levofloxacin (18.2%) were the most commonly prescribed empirical therapy antibiotics. Interestingly, a study by Kotwani et al. reported a similar trend, with two antimicrobials from the same drug class being prescribed to the majority of patients. Moreover, Nayar et al. found in their study a preference for the combination of beta-lactam and macrolide antibiotics, particularly ceftriaxone and azithromycin. These findings align with our study's observations regarding prescribed antimircrobials. [10,11]

After getting result of culture and sensitivity reports, definitive therapy was promptly started for specific treatment based on the identified microorganism. It was noted that a significant number of cases of Streptococcus pneumoniae and Klebsiella pneumoniae showed resistance to first-line treatments, necessitating a shift to higher classes of antibiotics to which the organisms remained sensitive. Consequently, in this study, the most commonly prescribed drugs included levofloxacin (26.1%), ceftriaxone (18.2%), meropenem (12.6%), azithromycin (5.9%), amoxicillin-clavulanic acid, vancomycin, piperacillin-tazobactam, amikacin, clarithromycin, doxycycline, and cefoperazone. These findings align closely with those of the Kotwani et al. study, wherein cephalosporins followed by macrolides emerged as the most commonly prescribed antimicrobials, resembling the pattern observed in our study. Moreover, in the present study, antimicrobial agents were utilized

empirically in 57.3% and as definitive therapy in 31.3% of patients, a pattern bit similar to that reported in the Kotwani et al. study. [10]

The total duration of antimicrobial therapy as definitive treatment for hospitalized patients in this study was 4.47 ± 0.85 days, while the overall length of hospital stay was 8.60 ± 1.48 days. Interestingly, these findings closely resemble with those reported in studies conducted by Kotwani et al. and Nayar et al.[10,11]

Indeed, the route of administration of antimicrobial agents (AMAs) is typically determined by several factors, including the site and severity of the infection. [12] In this study, a majority of antimicrobials were administered intravenously (76.2%), while medications such as clarithromycin, ofloxacin, and azithromycin were given orally (23.8%) as definitive therapy. A study by Cyriac et al. delves into the policy regarding changing the route of drug administration. [13]

In 72.3% of patients, a combination of antimicrobial agents (AMAs) was utilized. Amikacin was included in cases of gram-negative infections to augment synergistic prolongation of the post-antibiotic effect of beta-lactams. However, the concurrent use of ceftriaxone with amoxicillin-clavulanic acid and piperacillin with carbapenems may not be deemed rational, as there is no documented advantage with these combinations. In this study, the most frequently employed drug combinations included amoxicillin-clavulanic acid with either azithromycin or levofloxacin. A similar pattern of fixed-dose combination (FDC) prescription was observed in the study conducted by Mahajan et al. [14] Beta-lactam in combination with fluoroquinolones and macrolides was prescribed in 4.1% of patients. Additionally, fluoroquinolones coupled with cephalosporins in 11% of patients were noted as being irrationally prescribed in empirical treatment.

In this study, the average number of drugs prescribed per patient was 6.57±2.17, with an average of 2.34±1.67 antibiotics per prescription. A critical indicator of prescription quality is the average number of medications per prescription. It is generally recommended to minimize this as much as possible, as higher numbers often correlate with increased risks of drug interactions, bacterial resistance, and elevated cost of hospital expenses. Upon thorough screening of prescriptions, it was observed that mono-antibiotic prescriptions accounted for 35 (15.3%) instances, while poly-antibiotic therapy was prescribed in 195 (84.7%) cases. This presentation highlights the prevalence of poly-antibiotic prescriptions over mono-antibiotic therapy. Studies conducted by Mehrad et al. in 2015 and Bala et al. in 2009 demonstrated matching prescribing indicators. [15,16]

In our study, approximately 40% of drugs were prescribed using their generic names, with the majority of medications being prescribed by brand names. However, it is noteworthy that prescribing medications by their generic names can facilitate better inventory monitoring by the hospital pharmacy. A study conducted by Mittal et al. revealed a similar pattern of prescribing, highlighting the importance of this practice in optimizing healthcare management. [17] The average number of prescriptions involving intravenous (IV) antimicrobials was 90.4%. Despite the option of an oral route, the majority of inpatients receive IV antibiotics for an extended duration which also raises concern.

Data on drug consumption was quantified in terms of fixed daily doses (DDD) per 100 bed days. Amoxicillin-clavulanic acid exhibited the highest value of 14.2 DDD per 100 bed days, indicating its status as the most commonly used broad-spectrum antibiotic, followed by azithromycin with a value of 12.6 DDD per 100 bed days in empirical therapy. In definitive therapy, the highest value was recorded for levofloxacin at 14.6 DDD per 100 bed days, followed by meropenem with a value of 13.1 DDD per 100 bed days. This pattern of drug utilization observed in our study is in line with findings reported in medical literature [18,19, 20] The consumption of antibiotics as definitive therapy was strongly correlated with the culture sensitivity report, with an overall DDD of 52.24 compared to 35.34 DDD/100 bed days for empirical therapy. This association can be attributed to the resistance observed against first-line drugs for BP. Consequently, patients had to shift to higher-class antibiotics, resulting in increased consumption of DDD. [21]

Conclusion

This research offers significant insights into the prescribing patterns of antimicrobial agents (AMAs), which can serve as a foundation for designing intervention studies aimed at promoting rational drug utilization. The findings of this study throw light on the typical patterns of antibiotic usage in Bacterial Pneumonia within medicine departments. Antibiotic resistance presents challenge for the medical community, with overuse, underuse and misuse of antibiotics being significant contributing factors. Given the paucity of data on antimicrobial usage patterns in our community. Drug Utilization Studies should be conducted across various departments in medical colleges and Institutes to assess antibiotic utilization comprehensively. An effective prescription audit should advocate for the rational use of reserve antibiotics and the efficient management of limited resources. Such studies would go a long way in achieving the much-needed concept of rational pharmacotherapeutics in the best interest of patients.

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