Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/sgynzz56

EVALUATE THE IMPACT AND CHALLENGES OF ANTIMICROBIAL RESISTANCE IN PNEUMONIA: A CROSS SECTIONAL STUDY IN TERTIARY CARE HOSPITAL

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Abstract

Background: The rise of antimicrobial resistance (AMR) poses a significant threat to treating infections like pneumonia. In Pakistan, limited access to culture and sensitivity tests often leads to unchecked infections. Therapy failure and frequent antibiotic switching signal drug resistance and AMR.

Objectives: The study underscores the need for optimized antibiotic use, improved diagnostics, and strategies to combat AMR. Effective solutions will help mitigate resistance, enhance treatment outcomes, and reduce the burden of infections.

MethodologyThe study analyzed 50 pediatric pneumonia cases to assess antibiotic prescription patterns, hospital stay duration, antibiotic consumption, switching, and patient discharge outcomes. This evaluation aimed to understand treatment approaches, identify potential areas for improvement, and optimize patient care**.**

Results: The study results showed that pneumonia is more common in children (1-5 years); n=20 (40%), followed by neonates (0-12 months); n= 16 (32%), respectively. Monotherapy was used upon initial admission of patients, while combination therapy and antibiotic switching occurred when patients didn't respond. Non-responsiveness prolonged hospital stays, suggesting drug-resistant bacteria.The average hospital stay was 6.5 days with monotherapy and 3.5 days with combination therapy. Cefoperazone (28%), meropenem (26%), and vancomycin/linezolid (20%) were the most prescribed antibiotics. Meropenem+linezolid (n=9) and meropenem+vancomycin (n=7) were common combinations.

Conclusion: The study reveals a concerning trend of drug-resistant bacterial strains causing pneumonia in pediatric patients, signaling a potential silent pandemic of antimicrobial resistance (AMR). This emerging threat requires careful monitoring and reporting to mitigate its consequences.

Key words: Antimicrobial resistance (AMR), Antibiotic switching, Monotherapy, Pneumonia.

INTRODUCTION

Pneumonia is a serious infectious disease that affects the lungs and can be life-threatening. It is an acute infection of the lung parenchyma caused by one or more pathogens and is a leading cause of illness and mortality worldwide, affecting people of all ages. According to the World Health Organization (WHO), pneumonia claims approximately 2.5 million lives annually predominantly in underdeveloped and low-income countries. An estimated 120 million children under 5 years old develop pneumonia each year, resulting in 1.3 million deaths. In 2017, pneumonia accounted for 15% of all pediatric deaths, with over 808,000 children under 5 years old succumbing to the disease. In Pakistan, pneumonia-related deaths range from 10% to 30%, with poorer access to healthcare contributing to higher mortality rates, particularly among early infants. Mortality rates vary by age: 3% for under-five-year-olds, 14% for those aged 5-65 years, and 24% for individuals over 65 years old.

Globally, an estimated 138 million pneumonia cases were reported in 2015. Pakistan is among the five countries bearing the burden of 49% of pneumonia-related deaths and 52% of all pneumonia cases, with approximately 58,000 under-five children dying from pneumonia annually.. According to the Demographic and Health Survey (2012-2017), 82% of children with acute respiratory infection symptoms, including pneumonia, sought medical treatment. Antimicrobial resistance (AMR) exacerbates pneumonia's impact, as drug-resistant bacterial strains render treatments ineffective. Pakistan faces significant AMR challenges, contributing to increased mortality, prolonged hospital stays, and higher healthcare costs. Globally, Antimicrobial resistance causes 700,000 deaths annually, projected to rise to 10 million by 2050 if unaddressed.To combat pneumonia and AMR, Pakistan must strengthen healthcare infrastructure, promote responsible antibiotic use, and enhance surveillance. Addressing these interconnected issues can reduce pneumonia's burden, mitigate AMR's impact and improve public health outcomes.

A study was carried out in China, when 106 private practitioners were asked to prescribe antibiotics for pulmonary tuberculosis (TB) patients, 63 different drug regimens were followed by the practitioners, out of these 63 only 6 were turned to be suitable. Usually, this resistance trend is much higher in low-income countries and developing nations of the world. Specifically, *Acinetobacter baumannii* has higher rates of resistance among other bacterial strands. Secondly, *Enterococcus faecium* (87%) is now resistant to broad spectrum penicillin's while *Klebsiella pneumoniae* is also highly resistant to various antibiotics. In addition, both of these bacterial strains are placed in priority list by WHO for development of new antibacterial agents for their prevention. n low- and middle-income countries (LMICs), inadequate healthcare infrastructure, limited access to quality treatments, and diagnostic gaps contribute to antibiotic misuse. This leads to higher morbidity and mortality rates. Key factors driving misuse include over-the-counter antibiotic sales without prescriptions or confirmatory tests, and inability to access quality antibiotics, exacerbating poverty-driven AMR. Poverty also hinders treatment compliance, promoting resistance through limited antibiotic exposure. Those in extreme poverty often rely on unlawful providers, obtaining inferior, counterfeit, or outdated medications, further fueling AMR. Addressing these interconnected issues is crucial to mitigating AMR's impact in LMICs.

After starting an antibiotic regimen (whether monotherapy or combination therapy), some patients show responsiveness to the antibiotics resulting in early discharge from the hospital within a week However, Some patients don't respond to initial antibiotic regimens, necessitating switching to another class, which prolongs hospital stays. This resistance, often indicative of drug-resistant bacterial strains, worsens patient outcomes.Assessing antibiotic resistance in pneumonia patients receiving therapy is crucial.

This study aimed to provide insights into effective pneumonia management, mitigate antimicrobial resistance, and enhance healthcare practices in Pakistan, ultimately reducing morbidity and mortality associated with pneumonia in children.

OBJECTIVES

The study's aim to evaluate antibiotic prescribing practices in pediatric pneumonia patients, assess therapy failure rates and identify contributing factors, examine patient responses to antibiotic treatment, identify patterns of antibiotic resistance and switching-over, and inform strategies to optimize antibiotic use and improve patient outcomes.

METHODOLOGY

A cross-sectional study was conducted at Dow University Hospital. The study analyzed 50 pediatric pneumonia cases to evaluate antibiotic prescription patterns. The study focused on pediatric wards, which have a high admission rate for pneumonia patients . A computer generated electronic list of admitted patients was shared by the admissions department daily. Patient profiles were reviewed and data were collected on the predesigned electronic form adapted from the questionnaire Main focus was shifted toward the antibiotic consumption and treatment regimen. Total number of antibiotics, monotherapy or combination therapy, hospital longevity, average stay in the hospital, antibiotic at which the patient was discharged and antibiotic switching-over were evaluated on a comprehensive designed proforma.

Ethical considerations

The study was approved by the institutional IRB of Dow University of Health Sciences.

Data management and statistical analyse

Questionnaire data were entered in Excel and transferred to STATA for analysis. Data analysis involved evaluating 50 pediatric pneumonia patient prescriptions, focusing on antibiotic consumption, hospital stay duration and treatment outcomes. Statistical analysis focused on descriptive statistics and frequency analysis to summarize data and identify trends in antibiotic use and resistance.

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RESULTS

This study analyzed 50 pediatric pneumonia patient prescriptions, revealing that (30)59% were male and (20) 41% female(fig 1), with neonates (45%) and children aged 1-5 years (40%) most prevalent. Pneumonia was common in children aged 1-5 years (40%) and neonates (32%) as shown in fig 2. Monotherapy was initially used, but combination therapy and switching occurred due to non-responsiveness, suggesting drug-resistant bacteria.

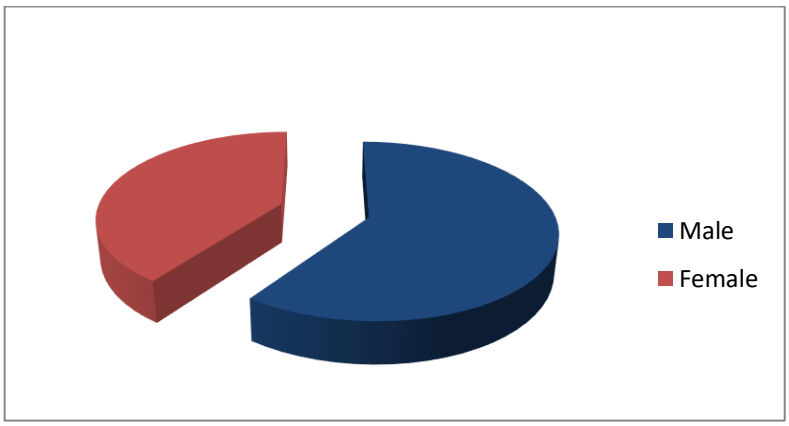

Fig 1:Gender wise distribution of pediatric pneumonia patients

The average hospital stay was shorter with combination therapy (3.5 days) vs. monotherapy (6.5 days). Meropenem+linezolid and meropenem+vancomycin were effective combinations. Cefoperazone, meropenem, and vancomycin/linezolid were frequently prescribed. These findings highlight the importance of tailored combination therapy in managing pediatric pneumonia and mitigating antimicrobial resistance.

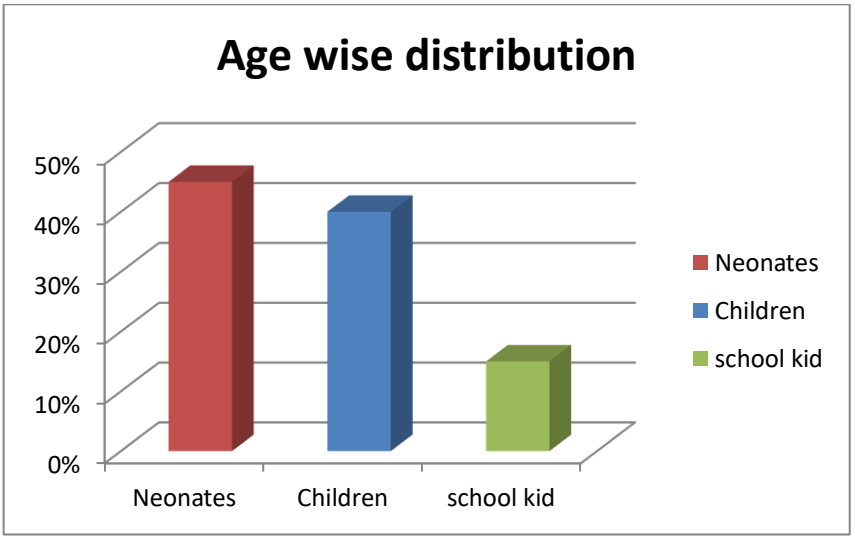

Fig 2:Age wise distribution of pediatric pneumonia patients

Patients admitted to the hospital hailed from different regions of Sindh. The majority were from Karachi (n=18, 30%), followed by Hyderabad (n=13, 21.6%), Sukkur, t (n=9, 15%), Badin (n=6, 10%), Shikarpur (n=4, 6.6%), and Mirpurkhas(n=3, 5% each), reflecting diverse pneumonia prevalence and healthcare access patterns.

This study revealed two antibiotic treatment scenarios: monotherapy and combination therapy. Initially, some patients received monotherapy, but others required combination therapy due to non-responsiveness. Effective combinations included Meropenem+Linezolid (Mer+Lin), Meropenem+Vancomycin (Mer+Van), Cefoperazone+Vancomycin (Cef+Van), and Cefoperazone+Linezolid (Cef+Lin).

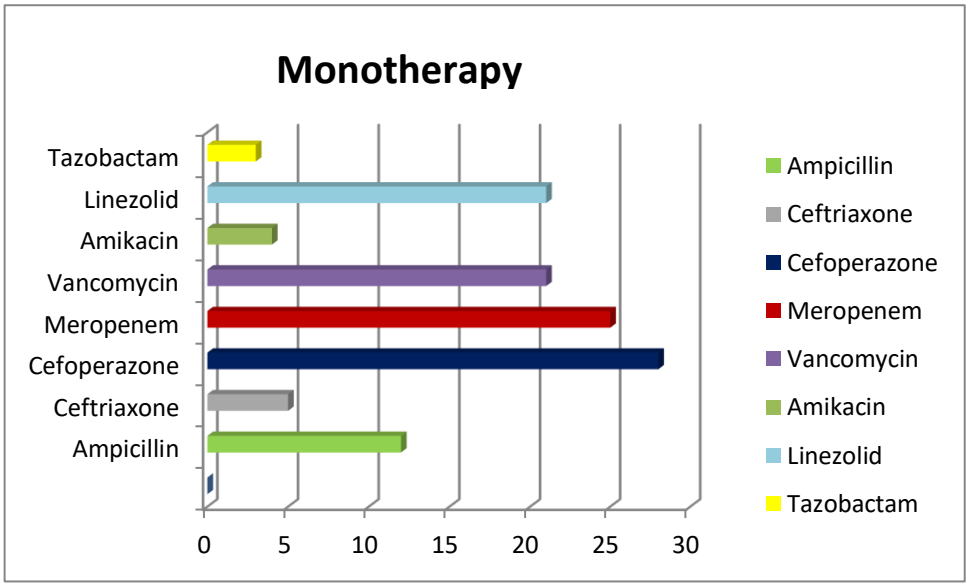

Fig 3: Overall antibiotic consumption as Monotherapy .

Only 5 of 35 patients receiving initial cefoperazone monotherapy were discharged, with an average 7.8-day hospital stay. Cefoperazone was ineffective for 30 patients, necessitating switching to other antibiotics or combinations like Mer+Lin, Mer+Van, Cef+Lin, and Cef+Van. Mer+Lin was the most effective regimen, discharging 10 patients with a 3-day average hospital stay Mer+Van also reduced hospital stays to 3 days.

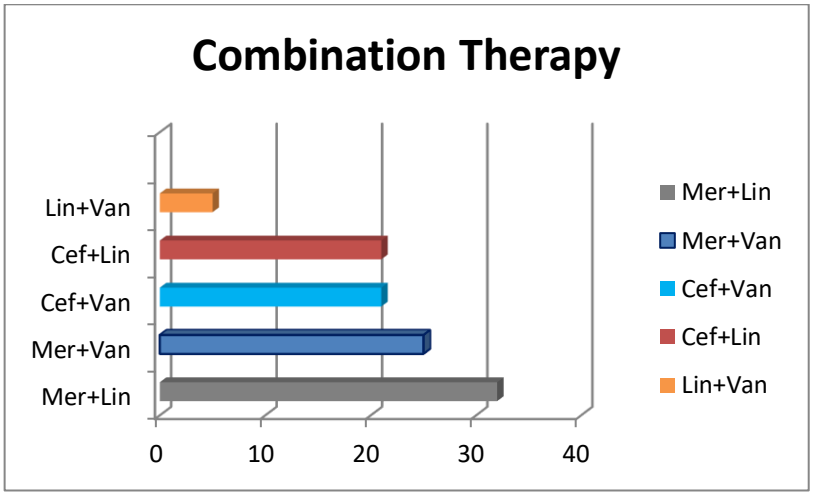

Fig 4: Overall antibiotic consumption as Combination therapy .

Other effective combinations included Cef+Lin and Cef+Van, with average stays of 3.5 days. These findings highlight the benefits of tailored combination therapy in managing pediatric pneumonia.
The study evaluated therapy failure and antimicrobial resistance (AMR) based on hospital stay and antibiotic switching. Patients discharged within 1-5 days (n=30, 60%) were considered responsive to antibiotics, mostly receiving combination therapy like cefoperazone+vancomycin, meropenem+linezolid, and cefoperazone+linezolid.

Table 1 showed the Antibiotic frequency and switching-over pattern

Antibiotic	Total No	Number of switching-over noticed for n=60 patients	%age
Ampicillin	2	2	**100**
Ceftriaxone	3	2	**66**
Cefoperazone	35	15	**42.8**
Meropenem	31	2	**6.4**
Vancomycin	24	1	**4.1**
Amikacin	2	0	**0**
Linezolid	24	0	**0**
Tazobactam	1	0	**0**
Total Number of antibiotics	**122**	**22**	

Switching occurred frequently with monotherapy antibiotics: cefoperazone (42.8%), ceftriaxone (66%), ampicillin (100%), and meropenem (6.4%). In contrast, amikacin, linezolid, and tazobactam were used till the end of therapy.
Prolonged hospital stays (6-10 days, n=20; 11-15 days, n=1; 6-24 days, n=3) indicated therapy failure and potential AMR. Monotherapy with cefoperazone, ampicillin, and ceftriaxone showed lower responsiveness compared to meropenem, vancomycin, linezolid and amikacin likely due to drug-resistant bacterial strains. These findings suggest that combination therapy is more effective in managing pediatric pneumonia, and highlight the need to address AMR in treatment strategies.

DISCUSSION

Pneumonia, a leading cause of morbidity and mortality, is exacerbated by antimicrobial resistance (AMR). In pediatric patients, AMR complicates treatment, increasing hospital stays and mortality risk. This study highlights the challenges of antimicrobial resistance in pediatric pneumonia, where ineffective initial therapy necessitates switching to alternative antibiotics.The emergence of multidrug-resistant (MDR) bacteria, such as Klebsiella pneumoniae poses significant threats. Combination therapy, like meropenem+linezolid, offers promise in addressing AMR, reducing hospital stays and improving outcomes. However, resistance patterns vary, emphasizing the need for tailored treatment approaches.

Antimicrobial resistance consequences include prolonged hospitalizations, increased healthcare costs, and heightened mortality risk. Understanding local resistance patterns and optimizing antibiotic use are crucial in combating antimicrobial resistance. This study underscores the importance of judicious antibiotic prescribing and the potential benefits of combination therapy in managing pediatric pneumonia amidst antimicrobial resistance challenges. This study analyzed 50 pediatric pneumonia patient prescriptions, comprising 59% males (n=30) and 41% females (n=20). Two treatment scenarios emerged: monotherapy and combination therapy. Monotherapy (e.g., cefoperazone) was initially preferred, but often required switching to combination therapy (e.g., meropenem+linezolid) due to ineffectiveness. This combination proved most effective, discharging 10 patients with a 3-day average hospital stay.Other effective combinations included meropenem+vancomycin (3-day average stay), cefoperazone+linezolid, and cefoperazone+vancomycin (3.5-day average stay).

Antimicrobial resistance was assessed based on hospital stay and switching. Patients on combination therapy (e.g., cefoperazone+vancomycin, meropenem+linezolid) had shorter stays (1-5 days).Switching occurred frequently with cefoperazone (42.8%), ceftriaxone (66%), and ampicillin (100%). Meropenem+linezolid and meropenem+vancomycin combinations showed promise in reducing hospital stays. These findings highlight the importance of tailored combination therapy in managing pediatric pneumonia and mitigating antimicrobial resistance.

A study analyzing Klebsiella pneumoniae strains found significant shifts in resistance patterns between 2018 and 2022. In 2018, 12.5% of strains were susceptible, 7.5% resistant, 17.5% multidrug-resistant (MDR), and 62.5% extensively drug-resistant (XDR). These strains showed high resistance rates to amoxicillin/clavulanic acid (90%), ciprofloxacin (100%), piperacillin/tazobactam (92.5%), and cefoperazone/salbactam (95%). In contrast, the 2022 group showed no susceptible strains, with 21.4% resistant, 7% MDR, and 71% XDR. Notably, resistance to amoxicillin increased significantly, from 10% in 2018 to nil in 2022. Overall, resistant Klebsiella pneumoniae rates rose from 7.5% in 2018 to 21.4% in 2022. Among mechanically ventilated ICU patients, XDR Klebsiella pneumoniae increased from 62.5% in 2018 to 71% in 2022, highlighting growing concerns about antimicrobial resistance.

The study revealed a concerning rise in extensively drug-resistant (XDR) Klebsiella pneumoniae, from 62.5% in 2018 to 71% in 2022. Monotherapy was often ineffective due to antimicrobial resistance (AMR), rendering first-line antibiotics less effective. Combination therapies showed promise, but bacteria may develop resistance through natural selection. To address this issue, in-depth studies are needed to identify root causes, implement preventive measures, and explore alternative antibiotics from natural sources. Leveraging modern technology can help combat this growing health threat. Urgent action is required to mitigate the impact of AMR and protect public health.

CONCLUSION

This study highlights the urgent issue of antimicrobial resistance (AMR) in pediatric pneumonia in Pakistan. Combination therapy, specifically meropenem+linezolid, proved effective in reducing hospital stays. The findings emphasize the need for responsive treatment approaches and contribute to understanding pediatric pneumonia and antimicrobial resistance. Further research is needed to determine the underlying causes of AMR in pediatric pneumonia. Preventive measures and alternative

antibiotic sources should be explored to minimize resistance. Leveraging innovative medical research and technology will be crucial in combating this silent pandemic and improving treatment outcomes for pediatric pneumonia patients.

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