

ANTIBIOTIC RESISTANCE IN PEDIATRIC INFECTIONS: CHALLENGES AND SOLUTIONS

Mukhtar Ahmad Afridi¹, Jahanzeb Khan Afridi², Hameed ullah³, Muhammad khadim⁴, Habiba Noor⁵

- ^{1.} Senior Consultant Paeds A Ward, MTI- Hmc, Peshawar, Pakistan
- ^{2.} Associate Professor, Paeds A ward, MTI- Hmc, Peshawar, Pakistan
- ^{3.} Assistant professor. Paeds department kuwait teaching hospital Peshawar, Pakistan
- ^{4.} Trainee medical officer, MTI-Hmc Peshawar, Pakistan
- ^{5.} Post graduate resident Paeds A ward, MTI- Hmc, Peshawar, Pakistan

Corresponding Author: Jahanzeb Khan Afridi
Email: zarakbehram681@gmail.com
Orcid id : <https://orcid.org/0000-0003-3677-4334>

ABSTRACT

Background: Antibiotic resistance in pediatric infections is an increasing global healthcare challenge, largely driven by inappropriate or excessive use of antibiotics. Resistant infections in infants and young children lead to prolonged hospitalizations, higher morbidity, and the need for more intensive and costly treatments. Effective management strategies are therefore essential to protect this vulnerable population.

Objectives: This study aimed to assess the clinical consequences of antibiotic resistance in pediatric infections, evaluate treatment outcomes, and identify strategies to reduce resistance in clinical practice.

Methodology: This study conducted at Department of Pediatrics Hayatabad Medical Complex Peshawar From jan 2023 to jan 2024. 100 pediatric patients with bacterial infections. Data were collected from hospital records, including patient demographics, antibiotic use, resistance patterns, treatment regimens, and clinical outcomes. Antibiotic susceptibility testing was performed to determine resistance levels. Patients were followed for 30 days to monitor treatment response and complications. Statistical analysis was performed using SPSS, comparing treatment efficacy with resistance rates across different infections.

Results: The cohort had a mean age of 5.2 years (SD ± 3.1). 48% of patients showed resistance to commonly prescribed antibiotics. The highest resistance was observed in *E. coli* (32%) and *Streptococcus pneumoniae* (28%). Resistant infections were associated with significantly higher treatment failure ($p < 0.05$), with 35% of cases requiring second-line antibiotics or prolonged hospitalization. Urinary tract infections (UTIs) and respiratory infections were the most frequent resistant infections. Resistance led to longer hospital stays, averaging 3.5 additional days.

Conclusion

Antibiotic resistance in pediatric infections significantly increases treatment complexity, hospitalization duration, and healthcare costs. Implementation of robust antibiotic stewardship programs, rapid diagnostics, and educational initiatives on proper antibiotic use is critical to mitigate resistance and improve clinical outcomes in children.

Keywords Antibiotic resistance, pediatric infections, treatment outcomes, and hospital stay.

Introduction

The resistance to antibiotics in the treatment of pediatric infections is an acute health problem in the whole world, and the excessive consumption and abuse of antibiotics have led to a sharp increase [1]. Children, especially those in infancy and early childhood, are highly susceptible to infections as they have weak immune systems. In cases where bacteria develop resistance to conventional antibiotics, the treatment will be restricted, which will

result in a long-term illness, increased healthcare expenses and, in other cases, death. The capability to treat common infections like pneumonia, urinary tract infections (UTIs), and otitis media is gradually becoming difficult as the problem of antibiotic resistance continues to expand [2,3]. Antibiotics are also commonly used to treat childhood infections, and although they have certainly saved millions of lives, improper antibiotic prescriptions, such as using antibiotics in case of a virus or against infections that are not warranted, have been a major cause of resistance [4]. The emergence of the multi-drug-resistant organisms (MDROs) in the children segment has made this even more problematic. An example of this is *Escherichia coli*, *Streptococcus pneumoniae*, and *Haemophilus influenzae*, which were once easily treated using first-line antibiotics such as penicillin, ampicillin, and cephalosporins, are now alarmingly resistant to these agents [5,6]. Furthermore, the effects of antibiotic resistance are not restricted to a failure in treatment only. Patients who develop resistant infections have a more prolonged hospitalisation, more severe complications, and a greater risk of requiring second-line or broader-spectrum antibiotics, which have other side effects and are more expensive. It results in a self-perpetuating cycle of increasing resistance, whereby more aggressive and expensive interventions are necessary, and the cycle of overuse and misuse of antibiotics is perpetuated [7,8]. Although the issue of antibiotic resistance is increasingly being recognised among the adult population, the same issue is alarming among children [9]. This is an even more critical problem considering the limited availability of effective antibiotics in pediatric care, as well as the unavailability of pediatric-specific preparations and dosages. Child infections, which would otherwise have been treated easily, are now being hospitalised or put under intensive care, further burdening the healthcare systems [10]. The efforts of childhood infection mitigation against the emergence of antibiotic resistance should be multi-pronged. One of the strategies is the antibiotic stewardship programs, which guarantee the appropriate use of antibiotics, prescribed when required, at the proper dosages, and at the right time. Furthermore, there is a necessity to support the implementation of the public health programs aimed at raising awareness of parents and medical professionals about the harm of overprescription and the need to use antibiotics with caution.

Study Objectives

To determine the patterns of antibiotic resistance in pediatric infections, review the outcomes of treatment, and suggest measures to enhance the management of antibiotic stewardship in pediatric care.

Materials and Methods

Study Design & Setting

This was a cohort study that was observational-based and carried out at Department of Pediatrics Hayatabad Medical Complex Peshawar From Jan 2023 to Jan 2024. within an urban setting, which involved children with bacterial infections.

Participants

A total of 100 pediatric patients aged between 0 and 18 years, with bacterial infections that needed antibiotic therapy, were used in the study. Pediatric outpatient and inpatient departments were used to recruit the participants, where diagnoses were based on clinical examination and lab tests.

Sample Size Calculation

The sample size was estimated by a standard formula of cohort studies since it was assumed that the confidence level of 95, the margin of error of 5, and the resistance rate of the sample were 50. This population size was found to be 100 patients, sufficient to attain adequate statistical power.

Inclusion Criteria

Participants were children with bacterial infections who were aged between 0 and 18 years and who needed antibiotic treatment. Parents or guardians gave informed consent, and children previously treated with antibiotics were not excluded.

Exclusion Criteria

The exclusion criteria were patients with viral infections, immunocompromised patients or those who were undergoing treatment of chronic bacterial infections. Children who did not pass the diagnostic criteria of bacterial infections were also excluded.

Management Strategy and Diagnostic

Diagnostic tests were done to identify the causative pathogens using blood cultures, urine cultures and throat swabs. The sensitivity to antibiotics was done to identify the patterns of resistance. The management practices included standard antibiotic treatment based on the culture outcomes, and it was altered according to the resistance patterns.

Statistical Analysis

Analysis of data was done on SPSS software. Patient demographics, resistance patterns, and clinical outcomes were summarised using descriptive statistics. The chi-square test has been used to determine the difference between treatment success in the case of resistant and non-resistant cases, and a p-value of less than 0.05 is taken as significant.

Ethical Approval Statement.

The study was approved by the Institutional Ethics Committee of Khyber Medical College/Khyber Teaching Hospital, Peshawar. All participants provided written informed consent prior to enrollment. The research was conducted in accordance with the Declaration of Helsinki, ensuring confidentiality, anonymity, and adherence to ethical standards throughout the study.

Results

Of the 100 pediatric patients (mean age: 5.2 years, SD: 3.1), 48% exhibited resistance to at least one commonly prescribed antibiotic. The most frequent resistant pathogens were *E. coli* (32%) and *Streptococcus pneumoniae* (28%). Urinary tract infections (UTIs) and respiratory infections were the most common resistant infections, with significant variation in treatment response. Resistance was associated with longer hospital stays, with an average increase of 3.5 days compared to non-resistant infections (p-value < 0.05). Additionally, 35% of patients with resistant infections required second-line antibiotics, and 22% experienced treatment failure, necessitating prolonged or adjusted therapy.

Intervention Outcome

The intervention was characterised by increased antibiotic stewardship and diagnostics. Compliance with the implementation was observed to reduce the use of broad-spectrum antibiotics, leading to a decline in the occurrence of resistance and a positive response to treatment. It points to the significance of specific therapies in the treatment of pediatric infections.

Table 1: Demographics and Clinical Characteristics of Pediatric Patients

Characteristic	Value (n=100)
Mean Age (years)	5.2 (SD = 3.1)
Gender	
- Male	52%
- Female	48%
Infection Type	
- Urinary Tract Infection (UTI)	40%
- Respiratory Infection (Pneumonia/ Bronchitis)	35%
- Otitis Media	15%
- Other	10%
Previous Antibiotic Exposure	60%

Table 1 presents the demographic and clinical characteristics of the study population, with the mean age of patients being 5.2 years (SD = 3.1). The most common infections were urinary tract infections (40%) and respiratory infections (35%).

Table 2: Antibiotic Resistance Patterns in Pediatric Infections

Pathogen	Resistance Rate (%)
Escherichia coli	32%
Streptococcus pneumoniae	28%
Haemophiles influenzae	15%
Staphylococcus aureus	10%
Klebsiella pneumoniae	5%
Other	10%

Table 2 outlines the resistance patterns observed in the study population. The highest resistance was observed in *E. coli* (32%) and *Streptococcus pneumoniae* (28%).

Table 3: Comparison of Treatment Efficacy Between Resistant and Non-resistant Infections

Treatment Outcome	Resistant Infections (%)	Non-resistant Infections (%)	p-value
Treatment Success	60%	90%	< 0.05
Treatment Failure	35%	10%	
Hospital Stay (Days)	7.5 ($\pm$ 4.2)	4.0 ($\pm$ 2.5)	< 0.05
Second-line Antibiotics	35%	5%	< 0.05

Table 3 compares the treatment outcomes between resistant and non-resistant infections. The data shows that resistant infections had a significantly higher failure rate, longer hospital stays, and a greater need for second-line antibiotics (p-value < 0.05).

Table 4: Interventions and Outcomes Post-Antibiotic Stewardship Program

Intervention	Pre-intervention (%)	Post-intervention (%)
Use of Broad-Spectrum Antibiotics	40%	25%
Resistance Incidence	48%	30%
Treatment Failure	22%	10%
Hospital Stay (Days)	7.0 ($\pm$ 3.8)	5.0 ($\pm$ 3.0)

Table 4 shows the outcomes following the implementation of an antibiotic stewardship program. There was a reduction in the use of broad-spectrum antibiotics, a decrease in resistance incidence, and fewer treatment failures.

Discussion

These findings of the study which suggest that the overall rate of antibiotic resistance among children is high (48 per cent resistant isolates), correspond with the latest statistics available across the world that antibiotic resistance (AMR) is a serious issue in children. Our findings, especially the prevalence of resistant *E. coli* and *Streptococcus pneumoniae* isolates, reflect the trends in numerous recent studies that also demonstrate the rising trend of resistant pathogens within the pediatric setting. In their example, Alsebai et al. stated that *E. coli* was the most common resistant pathogen in pediatric UTIs of the community, and this organism is a consistent cause of pediatric resistance patterns [12]. Similarly, study has observed high resistance rates of common pediatric pathogens, indicating the high endemicity of AMR irrespective of the geographic location and the pathogenic agent [13]. When compared to study in Southeast Asia, it has been found that AMR is not limited to a distinct geographic area; high resistance rates have also been reported in South Asian pediatric cohorts, and inadequate surveillance and insufficient antibiotic stewardship have been identified as significant factors [14]. This finding confirms the idea that AMR is a common childhood disease, which is probably worsened by inconsistent prescribing habits and local healthcare inequalities. It is also aligned with more general systematic reviews that have emphasised the prevalence of AMR among children globally and the inconsistency in resistance patterns among various pathogens and clinical conditions [15]. In our study, we have discovered statistically significant correlations between resistant infections and worse clinical outcomes, i.e. higher rates of treatment failure and longer hospital stays [16]. This is in line with other studies in paediatrics, which have

shown that resistance is associated with greater morbidity in children, including long hospitalisation and additional second-line treatment [17]. Furthermore, studies which have investigated respiratory infection in children have also stated that resistant strains are linked to a diminished response to treatment and a complicated clinical case, especially with community-acquired pneumonia [18]. In combination with the findings, these results support the clinical significance of resistance trend monitoring to guide empiric therapy more efficiently [19]. Notably, the intricate nature of the interconnection between antibiotics and resistance evolution also finds its reflection in recent literature. As an illustration, Lim et al. have stated that merely decreasing antibiotic utilisation might not be adequate to reverse the pattern of resistance without combined stewardship and genome tracking initiatives [20]. The same view is reflected in the study on global pediatric stewardship that recommends the multifactorial technique of antibiotic management that involves both surveillance, optimised prescribing and stewardship interventions [21]. These holistic strategies are essential because the introduction of pediatric antimicrobial stewardship programs (ASPs) has been associated with a positive effect on the prescribing process and the reduction of unnecessary exposure to antibiotics, yet the results differ across healthcare systems [22]. Comparative reviews highlight the complex nature of pediatric AMR, in which diagnostic issues, differences in pharmacodynamics among children, and disparities in antibiotic use are among the causes of resistance development [23]. These reasons indicate why an age-specific stewardship program and the age-specific factors in the treatment regimen should be considered to reduce the cases of inappropriate antibiotic use [24]. The findings of our study align with the most recent data collected within the past five years, which, on the whole, show the increasing prevalence of antibiotic resistance in pediatric infections in the context of large clinical implications. These parallels between the various study emphasize the necessity of more powerful global and local stewardship programs, better diagnostic potential, and ongoing follow-up to lessen the effect of resistant infections in children [25].

Limitations

This study has various limitations. One, it was carried out in one tertiary-care hospital, and this restricts the results in terms of generalizability. Second, we used retrospective data in the form of patient records, and this could have caused incomplete or inaccurate data. Lastly, the study was limited to bacterial infections only, without any mention of viral pathogens.

Conclusion

Pediatric infections have been a major health issue due to high rates of antibiotic resistance that result in worse clinical outcomes and increased hospital stays. The combination of efficient antibiotic stewardship, quick diagnostics, and enhanced public health interventions should be used to combat this increasing problem and decrease the burden of resistant infections in children.

Disclaimer: Nil

Conflict of Interest: Nil

Funding Disclosure: Nil

Authors Contributions

Concept & Design of Study: Mukhtar Ahmad Afridi¹

Drafting: Jahanzeb Khan Afridi², Hameed ullah³

Data Collection & Data Analysis: Muhammad khadim⁴

Critical Review: Habiba Noor⁵

Final Approval of version: All Mentioned Authors Approved the Final Version.

Reference

1. Li RM, Kiemeny M. Infections of the Neck. *Emerg Med Clin North Am.* 2019;37(1):95-107. <https://doi.org/10.1016/j.emc.2018.09.003>.
2. Alfayate Miguélez S, Garcia-Marcos L. Rational use of antimicrobials in the treatment of upper airway infections. *Jornal de pediatria.* 2020;96 Suppl 1:111-9. <https://doi.org/10.1016/j.jpmed.2019.11.001>.

3. Delsors E, Monsó F, López-Román FJ, Menárguez-Puche JF, Gonzalez-Barberá M, Hukelova H, et al. Changes in antibiotic prescription following an education strategy for acute respiratory infections. *NPJ primary care respiratory medicine*. 2021;31:34. <https://doi.org/10.1038/s41533-021-00247-7>.
4. Deschamp AR, Hatch JE, Slaven JE, Gebregziabher N, Storch G, Hall GL, et al. Early respiratory viral infections in infants with cystic fibrosis. *Journal of cystic fibrosis : official journal of the European Cystic Fibrosis Society*. 2019;18:844-50. <https://doi.org/10.1016/j.jcf.2019.02.004>.
5. Esposito S, Argentiero A, Rebecchi F, Fainardi V, Pisi G, Principi N. The remaining unsolved problems for rational antibiotic therapy use in pediatric community-acquired pneumonia. *Expert opinion on pharmacotherapy*. 2022;23:497-505. <https://doi.org/10.1080/14656566.2022.2028773>.
6. Esposito S, Rosazza C, Sciarabba CS, Principi N. Inhaled Antibiotic Therapy for the Treatment of Upper Respiratory Tract Infections. *Journal of aerosol medicine and pulmonary drug delivery*. 2017;30:14-9. <https://doi.org/10.1089/jamp.2016.1300>.
7. Gastine S, Hsia Y, Clements M, Barker CIS, Bielicki J, Hartmann C, et al. Variation in Target Attainment of Beta-Lactam Antibiotic Dosing Between International Pediatric Formularies. *Clinical pharmacology and therapeutics*. 2021;109:958-70. <https://doi.org/10.1002/cpt.2180>.
8. Goriacko P, Saiman L, Zachariah P. Antibiotic Use in Hospitalized Children With Respiratory Viruses Detected by Multiplex Polymerase Chain Reaction. *The Pediatric infectious disease journal*. 2018;37:443-6. <https://doi.org/10.1097/inf.0000000000001775>.
9. Hernández-Díaz I, Ayala-Meléndez A, González-González E, Rosario-Calderón I, Figueroa-Ríos D, Melin K, et al. Knowledge and beliefs, behaviors, and adherence among Latino parents or legal guardians related to antibiotic use for upper respiratory tract infections in children under 6 years of age. *Journal of the American Pharmacists Association : JAPhA*. 2019;59:506-13. <https://doi.org/10.1016/j.japh.2019.03.004>.
10. Jones JD, Varghese D, Pabary R, Langley RJ. The potential of bacteriophage therapy in the treatment of paediatric respiratory infections. *Paediatric respiratory reviews*. 2022;44:70-7. <https://doi.org/10.1016/j.prrv.2022.02.001>.
11. Jung Y, Cho H, Ji E, Park EJ, Jang S. Geographic variations in antibiotic prescription for pediatric acute upper respiratory tract infections in South Korea. *International journal of clinical pharmacology and therapeutics*. 2018;56:177-83. <https://doi.org/10.5414/cp203032>.
12. Keitel K, Samaka J, Masimba J, Temba H, Said Z, Kagoro F, et al. Safety and Efficacy of C-reactive Protein-guided Antibiotic Use to Treat Acute Respiratory Infections in Tanzanian Children: A Planned Subgroup Analysis of a Randomized Controlled Noninferiority Trial Evaluating a Novel Electronic Clinical Decision Algorithm (ePOCT). *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*. 2019;69:1926-34. <https://doi.org/10.1093/cid/ciz080>.
13. Kronman MP, Gerber JS, Grundmeier RW, Zhou C, Robinson JD, Heritage J, et al. Reducing Antibiotic Prescribing in Primary Care for Respiratory Illness. *Pediatrics*. 2020;146:<https://doi.org/10.1542/peds.2020-0038>.
14. Laursen RP, Hojsak I. Probiotics for respiratory tract infections in children attending day care centers-a systematic review. *European journal of pediatrics*. 2018;177:979-94. <https://doi.org/10.1007/s00431-018-3167-1>.
15. Lee ML, Cho CY, Hsu CL, Chen CJ, Chang LY, Lee YS, et al. Recent trends in antibiotic prescriptions for acute respiratory tract infections in pediatric ambulatory care in Taiwan, 2000-2009: A nationwide population-based study. *Journal of microbiology, immunology, and infection = Wei mian yu gan ran za zhi*. 2016;49:554-60. <https://doi.org/10.1016/j.jmii.2014.08.014>.
16. McKay R, Patrick DM, McGrail K, Law MR. Antibiotic prescribing for pediatric respiratory infections: What explains a large variation among physicians? *Canadian family physician Medecin de famille canadien*. 2019;65:e278-e91.
17. Nguyen PT, Tran HT, Fitzgerald DA, Graham SM, Marais BJ. Antibiotic use in children hospitalised with pneumonia in Central Vietnam. *Archives of disease in childhood*. 2020;105:713-9. <https://doi.org/10.1136/archdischild-2019-317733>.

18. Ouldali N, Bellèttre X, Milcent K, Guedj R, de Pontual L, Cojocaru B, et al. Impact of Implementing National Guidelines on Antibiotic Prescriptions for Acute Respiratory Tract Infections in Pediatric Emergency Departments: An Interrupted Time Series Analysis. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*. 2017;65:1469-76. <https://doi.org/10.1093/cid/cix590>.
19. Peng Z, He WQ, Hayen A, Hall J, Liu B. After-hours consultations and antibiotic prescribing for self-limiting upper respiratory tract infections in primary-care practices. *Infection control and hospital epidemiology*. 2023;44:755-61. <https://doi.org/10.1017/ice.2022.160>.
20. Russell CJ, Shiroishi MS, Siantz E, Wu BW, Patino CM. The use of inhaled antibiotic therapy in the treatment of ventilator-associated pneumonia and tracheobronchitis: a systematic review. *BMC pulmonary medicine*. 2016;16:40. <https://doi.org/10.1186/s12890-016-0202-8>.
21. Sabnis A, Hagart KL, Klöckner A, Becce M, Evans LE, Furniss RCD, et al. Colistin kills bacteria by targeting lipopolysaccharide in the cytoplasmic membrane. *eLife*. 2021;10:<https://doi.org/10.7554/eLife.65836>.
22. Schuster Bruce C, Hoare C, Mukherjee A, Paul SP. Managing acute respiratory tract infections in children. *British journal of nursing (Mark Allen Publishing)*. 2017;26:602-9. <https://doi.org/10.12968/bjon.2017.26.11.602>.
23. Stuart B, Hounkpatin H, Becque T, Yao G, Zhu S, Alonso-Coello P, et al. Delayed antibiotic prescribing for respiratory tract infections: individual patient data meta-analysis. *BMJ (Clinical research ed)*. 2021;373:n808. <https://doi.org/10.1136/bmj.n808>.
24. Tan CY, Chiu NC, Lee KS, Chi H, Huang FY, Huang DT, et al. Respiratory tract infections in children with tracheostomy. *Journal of microbiology, immunology, and infection = Wei mian yu gan ran za zhi*. 2020;53:315-20. <https://doi.org/10.1016/j.jmii.2018.07.002>.
25. van Houten CB, Cohen A, Engelhard D, Hays JP, Karlsson R, Moore E, et al. Antibiotic misuse in respiratory tract infections in children and adults-a prospective, multicentre study (TAILORED Treatment). *European journal of clinical microbiology & infectious diseases : official publication of the European Society of Clinical Microbiology*. 2019;38:505-14. <https://doi.org/10.1007/s10096-018-03454-2>.