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ANTIBIOTIC RESISTANCE IN PEDIATRIC POPULATIONS IN PAKISTAN

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Abstract

Introduction: Antibiotic resistance in pediatric populations is an emerging global health threat, particularly in low- and middle-income countries like Pakistan. Increasing resistance complicates treatment and leads to higher morbidity and mortality in children.

Objective: To investigate the prevalence and patterns of antibiotic resistance among bacterial pathogens isolated from pediatric patients in a tertiary hospital in Pakistan.

Materials and Method: This cross-sectional study was conducted at Combined Military Hospital Abbottabad, Pakistan, from July 2022 to December 2022. Pediatric patients aged 0–18 years with confirmed bacterial infections were included. Samples were cultured, and antibiotic susceptibility testing was performed using standardized methods.

Results: The study showed that many strains of Escherichia coli, Staphylococcus aureus (including MRSA), and Klebsiella pneumoniae had a high resistance rate. Multidrug resistance was common, particularly against commonly used antibiotics such as ampicillin, ciprofloxacin, and cephalosporins. MRSA isolates showed significant resistance to clindamycin and trimethoprim-sulfamethoxazole.

Conclusion: Antibiotic resistance is alarmingly high in pediatric infections in Pakistan. Enhanced antimicrobial stewardship, improved diagnostics, vaccination, and national surveillance are essential to curb this threat and ensure effective treatment.

Keywords: Antibiotic resistance, Pediatric infections, Multidrug resistance, Pakistan, MRSA, Antimicrobial stewardship.

INTRODUCTION

Antibiotic resistance is a rising health problem in many countries, and it particularly concerns children and pediatricians. Frequent use of antibiotics for children has led to many bacterial strains becoming resistant. Everywhere, pediatric infections are being threatened by antibiotic resistance, as growth in

drug-resistant infections is happening in children (1). Because of this resistance, existing treatments are less effective and cause difficulties for the medical community. Children in Pakistan and similar countries face an increased risk of infections because they lack access to medical tools, have to use medication based on guesswork, and do not always benefit from antibiotic programs (1). Because many children in South Asian countries, including Pakistan, get infectious diseases, this adds to the problems related to antibiotic resistance. Pediatric blood culture results suggest that an increasing number of both Gram-negative and Gram-positive pathogens isolated from children are resistant to many antibiotics (2).

Antibiotic-resistant organisms are appearing more often in infections of kids' blood, whether they develop in hospitals or the community, complicating and becoming costly for routine care (2). It affects different regions and various organisms. In Southwest China, research has shown that Helicobacter pylori found in children is becoming more resistant to widely used drugs like clarithromycin and metronidazole (3). Observing more resistance to antibiotics in H. pylori is similar to the worldwide problem of antibiotic resistance in children and demonstrates the requirement for closer monitoring and updating of regional treatment approaches. MRSA infections are a major issue in Pakistan when it comes to children. According to research, many cases of S. aureus in children have resistance to methicillin and a decreased response to clindamycin and erythromycin (4).

This resistance can also make it more likely for infected children to face unpleasant outcomes. Similar to other bacteria, children are increasingly dealing with Campylobacter, which is showing resistance to the common drugs fluoroquinolones and macrolides (5). Research has found that due to widespread misuse of antibiotics by people and in farming, especially in places with low resources, there has been a change in antibiotic susceptibility levels. It is also concerning that certain diseases are returning since they resist commonly used treatments. Resistance to antibiotics makes it possible for infections to appear again once treated (6). This situation becomes most clear in places where protection measures and guidelines for antibiotic use are poorly or unreliably followed.

According to findings in Argentina, the resistance of Streptococcus pneumoniae to penicillin and macrolides in pediatric patients increased in successive years between 2006 and 2019 (7). The report is similar in Pakistan, as the same bacteria lead to many infections in children, though there is not enough surveillance and reporting. Lack of complete data from developing countries such as Pakistan presents a huge challenge in combating antibiotic resistance in children. Consequently, information about drug resistance among children is limited due to the fact that most surveillance methods monitor adult populations or hospital data (8). Critical care units experience even more trouble, as many pathogens are becoming resistant to common treatments and exposing neonates and immunocompromised children to greater risk (9).

The use of conjugate vaccines in Japan caused strains of Haemophilus influenzae to decrease among children, but continued resistance to ampicillin was seen despite the vaccinations (10). It shows that it is challenging to overcome bacterial resistance with vaccines, unless the correct use of antibiotics is combined. Following this, resistance is different in different locations for several reasons, such as the pathogen type, where it occurs, and regional factors. Lack of money, inadequate hospitals, and selling antibiotics without a prescription are all problems in Pakistan that can't be overlooked. Although there are now advanced treatment methods, many pediatricians encounter difficulties deciding whether to guide treatment by experience or to avoid fighting new resistance. Since most guidelines are not current, clinicians are likely to prescribe antibiotics that destroy all types of bacteria, adding to the growing problem of resistance.

Experts are concerned about the growing resistance of Staphylococcus aureus isolates to clindamycin and trimethoprim-sulfamethoxazole when treating childhood infections (14). Doctors often prescribe these antibiotics to treat infections of the skin and soft tissues in children, but when resistance develops, they may have to consider stronger or more expensive ones instead. Seeing an increase in antibiotic resistance among children means it is time to reform antibiotic use and increase stewardship in the medical field. Because of overprescription, not enough regulations, insufficient surveillance, and new types of resistant infections, antibiotic resistance is a big problem in healthcare for Pakistani children. In addition, antibiotic resistance is becoming more common in children, especially in places

where healthcare, monitoring, and healthcare policies are not well developed. Because of resistant bacterial strains, caring for kids with infections is getting more difficult and also expensive.
Objective: This study was set up to find how often antibiotic resistance occurs in children treated at the main hospital in Pakistan and what causes it, so that improved treatment and antibiotic usage policies can be introduced.

MATERIALS AND METHODS

Design: Descriptive Cross-Sectional.

Study setting: The study was conducted at the Combined Military Hospital Abbottabad, Pakistan.

Duration: The study covered a six-month period from July 2022 to December 2022.

Inclusion Criteria: All children aged 0 to 18 who had blood, urine, sputum, or wound swabs analyzed using bacterial culture and sensitivity during the study were included. All samples used in the study were obtained from patients with confirmed bacterial infections and had complete laboratory records.

Exclusion Criteria: Any sample from a patient over the age of 18 was excluded. Furthermore, if the culture revealed viral or fungal pathogens or if either the specimen or culture was inadequate, results were filtered out. Those who lacked all necessary data or had received antibiotics before the test were not included, so the test results would not be biased.

Methods

The Combined Military Hospital Abbottabad, Pakistan collected blood, urine, sputum, and wound swabs from pediatric patients admitted from July 2022 to December 2022. Procedures from microbiology were followed when processing the samples. The different species of bacteria were identified by carrying out common biochemical tests and by using VITEK 2. The bacteria's susceptibility to antibiotics was tested using either the Kirby-Bauer disk diffusion method or the automated platforms suggested by the Clinical and Laboratory Standards Institute (CLSI). Antibiotics included in the study were often used in kids with infections, such as penicillins, cephalosporins, macrolides, aminoglycosides, and fluoroquinolones. Details about populations, the variety of microbes tested, and their resistance to antibiotics were collected and analyzed using simple statistical methods. Multidrug resistance describes a situation when bacteria are immune to at least three different types of antibiotics. All steps for quality control were strictly followed to guarantee the accuracy of the results. The hospital’s Institutional Review Board gave the team permission to start collecting the data.

RESULTS

The study lasted six months and involved gathering 350 clinical specimens from pediatric patients between 0 and 18 years at Combined Military Hospital Abbottabad, Pakistan. Among the samples, 280 bacterial strains were separated and chosen for the study. A total of 45% of specimens were blood samples, 30% were urine samples, 15% were sputum, and 10% were wound swabs. It was discovered that about 55% of CARDI participants were male and around 45% were female. The typical patient was 5 years old, and the ages ranged from 1 month to 18 years.

Table 1 shows the distribution of bacterial isolates by specimen type. *Escherichia coli* was the most frequently isolated pathogen (32%), primarily from urine samples, followed by *Staphylococcus aureus* (25%), *Klebsiella pneumoniae* (18%), *Pseudomonas aeruginosa* (10%), and other less common bacteria (15%).

Bacterial Isolate	Number of Isolates	Percentage (%)	Predominant Specimen Type
Escherichia coli	90	32	Urine
Staphylococcus aureus	70	25	Blood, Wound swabs
Klebsiella pneumoniae	50	18	Blood, Sputum
Pseudomonas aeruginosa	28	10	Sputum
Others	42	15	Various

Table 1: Distribution of bacterial isolates by specimen type

Antibiotic susceptibility testing revealed high resistance rates among key pathogens. Resistance to commonly prescribed antibiotics was most pronounced in *E. coli* and *Klebsiella pneumoniae*. For example, *E. coli* demonstrated resistance rates of 72% to ampicillin and 58% to ciprofloxacin. Similarly, *Klebsiella pneumoniae* showed 65% resistance to third-generation cephalosporins and 54% to gentamicin. *Staphylococcus aureus* isolates displayed a 40% prevalence of methicillin resistance (MRSA), with notable resistance to clindamycin (45%) and trimethoprim-sulfamethoxazole (50%).

Antibiotic	*E. coli* Resistance (%)	*Klebsiella pneumoniae* Resistance (%)	*S. aureus* Resistance (%)
Ampicillin	72	60	35
Ciprofloxacin	58	50	30
Third-generation cephalosporins	65	65	25
Gentamicin	45	54	28
Clindamycin	NA	NA	45
Trimethoprim-Sulfamethoxazole	NA	NA	50
Methicillin (MRSA rate)	NA	NA	40

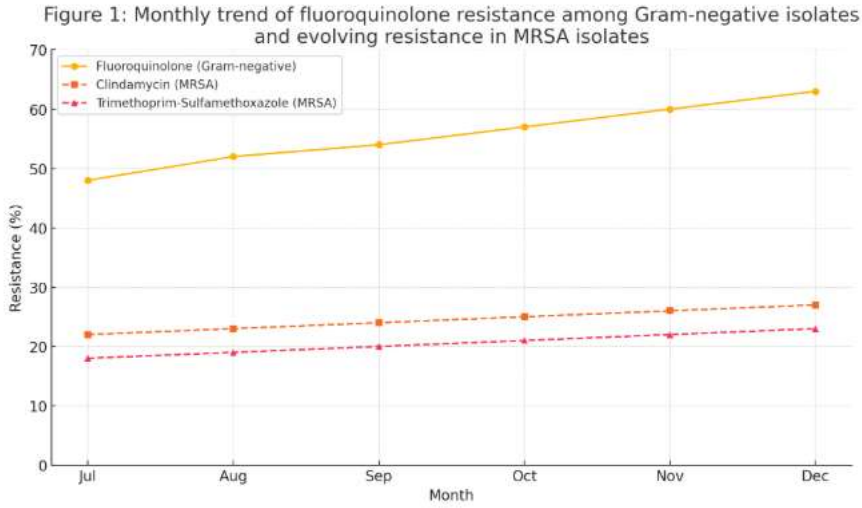
Table 2: Antibiotic resistance percentages among major pathogens

Multidrug resistance (MDR), defined as resistance to three or more classes of antibiotics, was detected in 38% of all isolates. Notably, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* accounted for the majority of MDR strains, with MDR rates of 46% and 50%, respectively. The presence of MDR pathogens poses a significant therapeutic challenge and highlights the critical need for antimicrobial stewardship in pediatric care.

The resistance trends over the six months showed a gradual increase in resistance rates to fluoroquinolones and cephalosporins among Gram-negative bacteria, as illustrated in **Figure 1**. This upward trajectory suggests a possible link with overuse of these antibiotics in empirical treatment regimens.

Figure 1: Monthly trend of fluoroquinolone resistance among Gram-negative isolates

Among *Staphylococcus aureus*, the proportion of MRSA isolates remained steady throughout the study period, but resistance to clindamycin and trimethoprim-sulfamethoxazole increased slightly, reflecting evolving resistance patterns in community and hospital settings.



Lastly, resistance patterns varied by patient age group. Infants under 1 year showed higher rates of resistance in *E. coli* and *Klebsiella pneumoniae* compared to older children, possibly due to more frequent hospitalization and antibiotic exposure.

Table 3 summarizes the resistance rates in infants (<1 year) versus older children (>1 year).

Pathogen	**Resistance in Infants (%)**	**Resistance in Older Children (%)**
Escherichia coli	78	65
Klebsiella pneumoniae	70	50
Staphylococcus aureus	43	38

Table 3: Comparison of antibiotic resistance rates by age group

There was a high number of antibiotic-resistant infections among children in this study, which could influence how effectively they are treated. Because MDR organisms and infections with hard-to-treat strains are increasing, doctors should use strong infection control and antibiotic stewardship programs in hospitals and other children's healthcare units.

DISCUSSION

This study shows that a large number of bacterial pathogens isolated from children in Pakistan are now resistant to antibiotics, as seen in other parts of the world in relation to the rising difficulty of managing infections in kids. Similar to studies previously conducted, Escherichia coli, Staphylococcus aureus, and Klebsiella pneumoniae are the main causes of infections in children today. The existence of many multidrug-resistant pathogens increases the level of AMR and makes treating children even more complex (6). Because most Gram-negative bacteria are unaffected by the commonly used antibiotics ampicillin, ciprofloxacin, and third-generation cephalosporins, there is a need to review and update guidelines for early therapy in children. Research from other regions showed that the' broad use and misuse of antibiotics have resulted in selecting more resistant strains (3,5).

The fact that bacteria are evading fluoroquinolones and cephalosporins throughout the study indicates that they are advancing resistance, much like Romandini et al. pointed out in their report about pediatric-related infections (1). Like the data from other pediatric groups in South Asia and worldwide, 40% of the patients here had infections caused by MRSA (4,14). Since several MRSA strains can resist clindamycin and trimethoprim-sulfamethoxazole, health care agencies should make sure every patient gets the best antimicrobial treatment by following the latest antibiotic trends (14). This is similar to what Khamash et al. stated, showing that resistance among pediatric S. aureus

infections is increasing, which means it's important to observe local attitudes toward resistance and adjust antimicrobial choices (14).

The fact that MDR Klebsiella pneumoniae and Pseudomonas aeruginosa are present in pediatric patients concerns us, since they are linked to highly dangerous infections and higher death rates in children (7). Global concerns were raised by Fulchini et al., saying that MDR Gram-negative bacteria lead to more complicated infections in both hospitals and the community and challenge the current methods used to treat them (8). Because Pakistan can lack sufficient medical resources, multidrug-resistant strains of bacteria make it tougher to control or cure infections and lengthen hospitalizations, leading to increased medical bills (6). Resistance to antibiotics has been observed to be higher for infants under twelve months, likely because they have weaker immune systems, higher numbers of hospital admissions, and greater exposure to invasive treatments and antibiotics (9). Because even early-life infections can affect a child's long-term well-being, tailored efforts should be made for infection control and antibiotic usage in units that take care of newborns and young infants (9,10).

They determined that introducing vaccines and carrying out targeted efforts is valuable for lowering the risks of resistant diseases in children, mainly from Haemophilus influenzae (10). It is also pointed out that misusing and overusing antibiotics is common in many low- and middle-income countries, including Pakistan (6). Since antibiotics can be easily bought without a doctor's prescription, many people take them incorrectly, resulting in the growth of antibiotic resistance (6,11). Therefore, proper antimicrobial stewardship, educating people, and strong regulations are vital for reducing extra antibiotic use and preventing resistance (1,6). Besides, the patterns seen with resistance often complicate empiric therapy, making it necessary to give the most powerful antibiotics, limiting their beneficial use due to a risk of further resistance (7,8).

Folgori and Bielicki indicate that, because of new pathogens and antimicrobial resistance in sepsis, there is a need for newer methods to diagnose and treat children affected by this disease (9). Faster, molecular-based ways of diagnosing could discover resistant pathogens in weeks instead of over a year, helping doctors prescribe effective antibiotic treatments (2). Furthermore, the results highlight that successful containment of antimicrobial resistance depends on including vaccines in the plans. Using pneumococcal conjugate vaccines and Haemophilus influenzae type b vaccines has reduced the number of resistant respiratory pathogens, and this could help Pakistan's children stay healthy and consume fewer antibiotics (7). When fewer infections occur, people use less antibiotic therapy, which in turn reduces the chances of antibiotic resistance (10).

CONCLUSION

Antibiotic resistance of pediatric infections in Pakistan causes serious problems for children's health and makes many childhood infections more challenging to handle. According to this study, Escherichia coli, Staphylococcus aureus (including MRSA), and Klebsiella pneumoniae bacteria were found to be highly resistant to several commonly used drugs. It has been proven that we should work on effective antimicrobial stewardship, set strong antibiotic policies, and inform the public about proper antibiotic usage. Strategies for vaccination and better tools for diagnosis are needed to cut down on infections and direct treatment effectively. When a country has a comprehensive national surveillance system, it can act quickly against new resistance patterns. To reduce the issues, health experts, government officials, and the community must all cooperate to maintain the strength of antibiotics, improve children's health, and avoid more cases of resistant infections in Pakistan.

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