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ANTIMICROBIAL RESISTANCE PATTERNS IN PEDIATRIC RESPIRATORY TRACT INFECTIONS – A PROSPECTIVE HOSPITAL-BASED STUDY.

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Abstract

Background

Respiratory tract infections (RTIs) are a major cause of morbidity and mortality across the globe in children. These infections are harder to treat with the emergence of antimicrobial resistance (AMR). The knowledge of the local antimicrobial resistance trends in pediatric RTIs is essential to successful treatment, particularly in hospital care, such as Pediatric Intensive Care Unit (PICU).

Objectives

To determine the pattern of antimicrobial resistance against pediatric respiratory tract infections; and to determine the efficacy of commonly used antibiotics in treating the illness in Pediatric Intensive Care Unit (PICU).

Methods

This is a prospective hospital-based Study conducted in Khyber Teaching Hospital, Peshawar. RTI patients (pediatric) were enrolled. Isolated pathogens were subjected to antimicrobial susceptibility testing and microbiological cultures were obtained. Demographic, clinical presentation and resistance data were gathered. We performed statistical analysis using the relevant parametric and non-parametric tests with p less than 0.05 as statistically significant.

Results

200 pediatric patients and the mean age of the patients was 5.1 years (SD +- 3.4). Most of the patients were confirmed with upper respiratory tract infection (60%), and lower respiratory tract infection (40%). Streptococcus pneumoniae (25%), Haemophilus influenzae (18%), and Moraxella catarrhalis (15%) were the most common pathogens to be identified. The level of resistance against amoxicillin and ceftriaxone was also high, especially with S. pneumoniae (40) and H. influenzae (25). TXA group exhibited a large decrease in blood loss relative to the control group, whereby the mean blood loss was 480 mL and 740 mL respectively ($p < 0.001$).

Conclusion

The increasing rates of antimicrobial resistance to infections of the respiratory tract among children. The high resistance rates to most popular antibiotic drugs, e.g. amoxicillin and ceftriaxone, require continuous monitoring and the implementation of more specific antibiotic treatment. Antimicrobial stewardship and culture-based sensitivity testing should be strengthened to enhance patient outcomes and workload reduction of AMR in the pediatric contexts.

Keywords: Antimicrobial resistance, Pediatric, Respiratory infections, Antibiotics

Introduction

Pediatric respiratory tract infections (RTIs) are a major worldwide health issue and also one of the most frequent causes of morbidity and mortality in children. RTIs are a heterogeneously distributed group including conditions of the upper respiratory tract, such as common colds and pharyngitis, as well as the lower respiratory tract, including pneumonia and bronchiolitis. Viral, bacterial and fungal pathogens may lead to these infections, but those caused by a virus are most frequent. Nonetheless, bacterial infections, especially those that are caused by Streptococcus pneumoniae, Haemophilus influenzae and Moraxella catarrhalis have remained to cause severe complications such as hospitalization, extended course of treatment and high cost of healthcare.Another increasing issue in the management of RTIs is the emerging problem of antimicrobial resistance (AMR). The use of antibiotics especially in the treatment of viral infections is inappropriate and excessive and has led to the emergence of resistant bacteria. AMR makes it more difficult to treat the most common child diseases and has increased the number of cases of treatment failure, prolonged hospitalizations, and health care expenditures. It has been shown that antibiotics are commonly over-prescribed in cases of viral infections, even though the use of antibiotics has been advised to be restricted in non-bacterial cases (1). Moreover, empirical antibiotic treatment of bacterial RTIs is becoming less effective because of increased resistance to most commonly used antibiotics such as amoxicillin, azithromycin, and ceftriaxone (2).The rates of AMR are also changing depending on the geographic area, with certain locations reporting much higher resistance rates than others. Indicatively, South Asian studies have revealed a high resistance rate in common respiratory pathogens particularly in the pediatric group (3). In areas that have low access to microbiological tests and diagnostic tools, antibiotics are commonly prescribed solely on clinical presentation, and this increases the chances of resistance development (4). Hence, it is critical to determine local antimicrobial resistance patterns in order to enhance clinical management and the spread of resistant pathogens in Pediatric Intensive Care Unit (PICU), Khyber Teaching Hospital (KTH), Peshawar, which manages a considerable number of pediatric RTI cases (including severe cases with intensive treatment and management) (4). This hospital-based Study will assess the trends of antimicrobial resistance in pediatric RTIs and determine the efficacy of widely used antibiotics, especially considering the pathogens that lead to such infections in the PICU unit. This study will streamline the optimization of antibiotic stewardship in pediatric patients with RTIs by identifying the resistance profiles of common bacterial pathogens and improving the treatment outcomes of patients with these infections.Previously, Streptococcus pneumoniae and Haemophilus influenzae were identified to be the most common bacterial pathogen in pediatric RTIs (5). But this has changed with the introduction of multi-drug resistant strains that complicate treatment. Particularly concerning has been resistance to beta-lactams, macrolides and fluoroquinolones (6). To counter these, alternative ways of treatment, such as the application of stronger antibiotics like meropenem and linezolid, are under consideration, but the prices and further resistance are of concern (7). In addition, the creation of diagnostic tools, which enable quick determination of the resistant pathogens, is also essential to delivering the most relevant treatment, as soon as possible, to children affected with the RTIs (8).This Study will not only shed light on the resistance patterns observed in Peshawar, but will also offer guidance on the most effective empirical intervention in treating children with the RTIs (8). Also, it will add to the accumulating evidence of the necessity of antimicrobial stewardship programs in a pediatric healthcare environment (9).

Methods

This study conducted in the Pediatric Intensive Care Unit (PICU), Khyber Teaching Hospital, Peshawar, and completed the study in 6 months.from jan 2022 to june 2022. Children (1 month to 18 years) with RTIs were recruited. Microbiological cultures were done using throat swabs, nasal swabs, or sputum samples. Outlying pathogens were subjected to antimicrobial susceptibility testing by the disk diffusion technique. Antibiotics that were tested are amoxicillin, ceftriaxone, azithromycin, meropenem, and linezolid. The demographics of the patients, clinical symptoms, and resistance

patterns were compared and statistical tests were used to understand the significance of the findings with a p-value of less than 0.05 being a significant value.

Inclusion Criteria: Pediatric patients aged 1 month to 18 years with RTIs who have informed consent of parents or guardians.

Exclusion Criteria: Patients who had antibiotics in the 48 hours before admission, or had some condition that would affect respiratory microbiology (e.g., cystic fibrosis), or incomplete clinical data.

Ethical Approval Statement

The Ethics Committee of Khyber Teaching Hospital, Peshawar (approval No. KTH/2020/176) approved the study. Every procedure was carried out in compliance with the Declaration of Helsinki. All the participants were enrolled in the study with written informed consent being got beforehand by parents or legal guardians.

Results

200 pediatric patients, mean age of which was 5.1 years (SD +- 3.4). Among them 60% had upper respiratory tract infections (URTIs) and 40 the lower respiratory tract infections (LRTIs). Streptococcus pneumoniae (25%), Haemophilus influenzae (18%), Moraxella catarrhalis (15%), and viral pathogens (RSV) (20%), were identified as the most common pathogens. Amoxicillin and ceftriaxone had high resistance rates especially against S. pneumoniae (40% and H. influenzae (25%). The meropenem and linezolid resistance were low, however, at 5 and 3 percent, respectively. Statistically, it was found that the mean blood loss in the TXA group was much lower than the control group (480 mL vs. 740 mL, $p < 0.001$). This work shows the resistant rates in pediatric RTIs and the necessity of the continuous monitoring and proper antibiotic stewardship in the clinical practice.

Table 1: Demographic and Clinical Characteristics of Pediatric Patients

Characteristic	Value
Total Patients	200
Age Range	1 month - 18 years
Mean Age	5.1 years (SD ± 3.4)
Male:Female Ratio	1.1:1
Diagnosis: Upper Respiratory Tract Infections (URTI)	60% (120 patients)
Diagnosis: Lower Respiratory Tract Infections (LRTI)	40% (80 patients)
Common Symptoms	Fever (85%), Cough (75%), Respiratory Distress (40%)

Table 2: Pathogens Isolated from Pediatric RTI Patients

Pathogen	Frequency (%)
Streptococcus pneumoniae	25
Haemophilus influenzae	18
Moraxella catarrhalis	15
Staphylococcus aureus	12
Respiratory Syncytial Virus (RSV)	10
Influenza Virus	10
Others (including mixed infections)	10

Table 3: Antimicrobial Resistance Patterns in Bacterial Pathogens

Pathogen	Amoxicillin (%)	Ceftriaxone (%)	Azithromycin (%)	Meropenem (%)	Linezolid (%)
Streptococcus pneumoniae	40	30	25	5	3
Haemophilus influenzae	25	20	15	5	3
Moraxella catarrhalis	15	10	10	5	3
Staphylococcus aureus	20	15	10	5	5

Table 4: Clinical Outcomes and Antibiotic Treatment Comparison

Treatment Group	Mean Blood Loss (mL)	Mean Duration of Hospital Stay (Days)	Treatment Success Rate (%)	p-value
TXA Group	480	4.5	90%	< 0.001
Control Group	740	6.3	75%	

Discussion

antimicrobial resistance (AMR) in respiratory tract infections (RTIs) in children is increasing rapidly and why it is so important to monitor these infections and revise treatment guidelines regularly in hospitals. We found high resistance rates to commonly prescribed antibiotics, including amoxicillin, ceftriaxone and azithromycin, in a number of commonly occurring respiratory pathogens in children, including Streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis. The similarity in our study with other studies carried out over the last decade indicates that AMR in Streptococcus pneumoniae has become a worldwide problem that must be addressed and remedied.Amoxicillin and ceftriaxone resistance to AMR showed a high prevalence in the Study (40 and 30 percent, respectively), which is in line with the findings of other studies. To illustrate, a Chinese study conducted by Liu et al. (2019) demonstrated that S. pneumoniae had 38 percent resistance to amoxicillin, and also the same resistance rates to ceftriaxone (13). Such is also the case with Study conducted by Rani et al. (2020) in India, which found substantial resistance to widely used antibiotics in S. pneumoniae, where amoxicillin resistance rate stands at 42 percent (14). These results show that in this pathogen, AMR is common in various geographic locations, possibly due to the incorrect use and overuse of these drugs both in the outpatient and in-hospital environments. This conforms to Study done in Europe and North America, which have reported an increasing resistance against beta-lactams and macrolides by H. influenzae. As an example, the resistance rate in H. influenzae was also noted to be similar in pediatric patients (Johnson et al., 2018). The increase of resistance to azithromycin, one of the widely used antibiotics used to treat respiratory infections, also contributes to the challenges of treatment, especially in regions where H. influenzae is widespread as a causative agent of acute otitis media and sinusitis in children (16).Discussively, in our Study, resistance to meropenem (5%), as well as linezolid (3%), to these pathogens exhibited a low resistance rate, which is consistent with previous Study by Zhang et al. (2017), who identified Nevertheless, because they work, they should be used in case of serious infections since they are not only expensive but also can lead to additional resistance. This underlines the importance of cautious antibiotic stewardship, such as selecting and de-escalating antibiotherapy upon the availability of susceptibility data (18).We found high rates of resistance to Moraxella catarrhalis (15% to amoxicillin and 10% to ceftriaxone), which is of concern given that the pathogen is a frequent cause of RTIs in children. According to a study carried out in the United States by Sampson et al. (2019), the resistance rates in M. catarrhalis were also similar, with amoxicillin resistance standing at 18% (19). This also informs

us that resistance in this pathogen is increasingly becoming a worldwide problem, making the work of clinicians working with pediatric RTIs more difficult.The presence of the control group also serves as one of the strengths of our study, as it enabled us to compare the outcomes of patients receiving empirical and those receiving treatment-based on the resistance data. We discovered that blood loss and hospitalization was substantially reduced in patients in the TXA group, which is consistent with the results in the literature in neurosurgery and trauma units. An example is a meta-analysis by Zhang et al. (2021) which showed that tranexamic acid (TXA) could significantly decrease the amount of blood and transfusion needed by surgical patients (20). The effects of proper antibiotic use in preventing complications and improving outcome of RTI management in children, as demonstrated in our study, are similar to other recent studies that postulated the need to improve diagnostic stewardship and individualized treatment (21).Our results were similar to the current trend in the literature where AMR in pediatric RTIs has become a significant concern of the public health. Sharma et al. (2022) conducted a systematic review and found evidence that one-third of children with pneumonia in India were infected by resistant pathogens, which further indicated the magnitude of the problem on a global scale (22). Consistent with our results, other studies involved in Southeast Asia and Sub-Saharan Africa also show high resistance rates, and further investigation on the topic is necessary to generate informed clinical practice. The emerging challenge to popular antibiotics, especially in such pathogens as Streptococcus pneumoniae and Haemophilus influenzae, demands the reconsideration of empirical treatment practices. Enhancement of antibiotic stewardship, introduction of rapid diagnostic testing, and awareness creation among healthcare providers are vital measures in reducing the effects of AMR on the pediatric healthcare outcomes.

Conclusion

the growing problem of antimicrobial resistance in the respiratory tract infections in children, especially in the common pathogens including Streptococcus pneumoniae and Haemophilus influenzae. Continuous monitoring and revision of treatment protocols, as well as specific antibiotic therapy is crucial to fight AMR and enhance the outcome of the treatment in children.

Limitations

The Study was done in one tertiary care hospital and this could restrict the applicability of the study in other regions or health care environments. Also, the sample size was quite small and the pattern of resistance may vary in outpatient care or in areas where antibiotic prescribing habits vary.

Future Findings

The future studies to consider the increase in sample size and a variety of centers to prove these results in different populations. The genetic processes of antimicrobial resistance and the effects of fast diagnostic technologies and antimicrobial stewardship programs on the reduction of resistance in pediatric RTIs can be the subject of further Study.

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