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A Meta-Analysis of Antibiotic Resistance Among Pediatric Populations Post-COVID-19 Infection

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Abstract:
Children are experiencing a disturbing surge in antibiotic resistance due to the COVID-19 pandemic, which has also caused public health concerns. This meta-analysis seeks to determine the prevalence of antibiotic resistance in children who have recovered from COVID-19. It is concerned with secondary bacterial infections and their impact on clinical outcome. Studies carried out between 2020 and 2023 reveal significant variations in resistance patterns across various regions. The prevalence of antibiotic resistance among common pathogens is different in rich and poor countries. The findings suggest that we must focus on improving antibiotic stewardship, diagnosing techniques, and monitoring to address the persistent issue of antibiotic resistance in children with COVID-19.

Keywords: Antibiotic resistance pediatric populations, COVID-19 meta-analysis, resistance patterns.

Introduction

Starting in December 2019, the COVID-19 outbreak has significantly altered the state of global health care, revealing and intensifying existing issues in healthcare systems.This is particularly distressing. Among these challenges, the prevalence of antibiotic-resistant bacterial infections has become a serious problem especially among vulnerable groups such as children (1). In the pandemic, antibiotics are used to control infections, both bacterial and viral, but their widespread use and indiscriminate use have increased resistance to these life-saving drugs. The impact of this phenomenon on children's health has been deemed particularly severe due to the need for antibiotics in their treatment of secondary infections caused by COVID-19 (2).

In this study, researchers explore the relationship between COVID-19 and antibiotic resistance in pediatric patients. The analysis examines the role of antibiotic mismanagement during the outbreak of the pandemic in promoting the development of resistant bacteria. By examining global data, the research seeks to measure resistance rates, identify the main causes of this trend, and evaluate the overall impact on children's health. These results offer useful lessons for managing this growing crisis and guiding future antibiotic management in the

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wake of a pandemic.

Materials and Methods

Search Strategy

To conduct this meta-analysis, a rigorous search of available literature was performed using multiple electronic databases, including PubMed, Scopus, Web of Science, and Google

Scholar. The inclusion criteria for studies were set to cover research conducted between January 2020 and December 2023. Studies were identified using search terms such as "antibiotic resistance," "COVID-19," "pediatric infections," "secondary bacterial infections," and "antibiotic stewardship," among others. In addition, references cited in selected articles were manually reviewed for further relevant studies.

Inclusion and Exclusion Criteria

The following criteria were used to select studies for inclusion in the meta-analysis:

Inclusion Criteria:

•Studies that focused on pediatric patients under 18 years of age.

•Studies that reported on secondary bacterial infections in children who had recovered from COVID-19.

•Research that provided data on antibiotic resistance in bacterial isolates from these pediatric patients.

•Peer-reviewed studies published in English.

Exclusion Criteria:

•Studies focusing exclusively on viral infections or those that did not provide information on antibiotic resistance.

•Animal studies, conference abstracts, and case reports.

•Studies that did not stratify data by pediatric age groups or did not offer antibiotic resistance data.

Data Extraction

The following key data were extracted from the included studies:

•Demographic information, including age and comorbidities of patients.

•The pathogens involved in secondary bacterial infections in children post-COVID-19.

•Antibiotic resistance data, including resistance to different classes of antibiotics (e.g., beta-lactams, fluoroquinolones, macrolides).

•Geographic location of the studies, categorized into low-income, middle-income, and high-income countries.

•Clinical outcomes such as length of hospital stay, recovery rates, and mortality.

•Information on antibiotic stewardship practices, where available.

Statistical Analysis

We used a random-effects meta-analysis to analyze the data. We aggregated resistance rates for different diseases and treatments, calculating 95% confidence intervals for each. The I^2 statistic helped us measure heterogeneity across the trials, allowing us to determine how much of the variance was due to heterogeneity instead of random chance. To understand the impact of healthcare infrastructure and geographical differences, we conducted subgroup analyses on antibiotic resistance patterns.

Results

Study Characteristics

A total of 22 studies were included in this meta-analysis, involving 5,400 pediatric patients who were diagnosed with COVID-19 and later developed secondary bacterial infections. These studies spanned various geographical regions, with 7 conducted in North America, 6 in Europe, 5 in Asia, and 4 in Africa. The average age of the pediatric patients was 7.5 years, and a significant number of cases were found in children under 5 years old. The findings indicated that secondary bacterial infections were identified in 28% of pediatric COVID-19 cases (Table 1).

Prevalence of Antibiotic Resistance

The most commonly identified pathogens in secondary bacterial infections among pediatric patients with COVID-19 were **Klebsiella pneumoniae**, **Escherichia coli**, **Pseudomonas aeruginosa**, and **Staphylococcus aureus**. Of the 5,400 pediatric patients analyzed, 32% had antibiotic-resistant infections, with resistance observed in varying degrees across different classes of antibiotics. The overall pooled resistance rate was 34%, which was higher than pre-pandemic rates of resistance in the same populations.

As shown in the table 2, **Klebsiella pneumoniae** and **Pseudomonas aeruginosa** exhibited the highest resistance rates, particularly against broad-spectrum antibiotics such as fluoroquinolones and third-generation cephalosporins.

Geographic Variation in Antibiotic Resistance

Regional differences in resistance were striking. Countries in **Africa** and **Asia** reported higher levels of resistance, particularly to **Klebsiella pneumoniae** and **Pseudomonas aeruginosa**, which are common pathogens in both community-acquired and healthcare-associated infections. These regions also demonstrated a higher proportion of **multidrug-resistant** (MDR) infections.

In contrast, **high-income countries** like the **USA**, **UK**, and **Germany** reported lower rates of resistance overall, which may be due to more stringent antibiotic stewardship practices and advanced

Table 1. Study Characteristics

Study	Region	Sample Size	Bacterial Pathogens Identified	Antibiotic Resistance Data Available
Smith et al. (2021)	USA	350	E. coli, Pseudomonas, Staphylococcus aureus	Yes
Chen et al. (2022)	China	450	Klebsiella pneumoniae, E. coli, Streptococcus pneumoniae	Yes
Patel et al. (2023)	India	300	Pseudomonas aeruginosa, Klebsiella, Streptococcus	Yes
Taylor et al. (2022)	UK	500	S. aureus, Pseudomonas aeruginosa, E. coli	Yes
Jackson et al. (2023)	South Africa	200	Klebsiella pneumoniae, Staphylococcus aureus	Yes

Table 2. Antibiotic Resistance Rates in Pediatric Populations Post-COVID-19

Pathogen	Resistance to Ampicillin (%)	Resistance to Trimethoprim-Sulfamethoxazole (%)	Resistance to Fluoroquinolones (%)	Resistance to Carbapenems (%)	Resistance to Third-Generation Cephalosporins (%)
Escherichia coli	28	22	17	7	21
Pseudomonas aeruginosa	40	15	35	13	25
Klebsiella pneumoniae	45	30	28	9	55
Staphylococcus aureus	12	10	6	0	2
Streptococcus pneumoniae	6	5	4	1	3

diagnostic capabilities. However, even in these countries, certain pathogens, such as **Pseudomonas aeruginosa**, showed concerning levels of resistance.

Impact on Clinical Outcomes

The presence of antibiotic resistance in pediatric patients with secondary bacterial infections following COVID-19 was associated with poorer clinical outcomes. The average length of hospital stay for children with resistant infections was 18 days compared to 11 days for children with non-resistant infections. Additionally, the mortality rate in the resistant group was 6.5%, compared to 2.1% in the non-resistant group.

Discussion

The results of this meta-analysis highlight several critical factors contributing to the rise in antibiotic resistance among pediatric populations following COVID-19 infections (3). The overuse and misuse of antibiotics during the pandemic are major drivers of this issue, which has been compounded by the uncertainty and challenges in distinguishing between viral and bacterial infections in pediatric COVID-19 cases (4). Throughout the pandemic, many clinicians opted to prescribe antibiotics empirically in cases of pediatric COVID-19, given the difficulty in promptly identifying bacterial co-infections (5). This practice, although aimed at preventing potential bacterial complications, has led to an increase in antibiotic resistance, as antibiotics are often unnecessary for viral infections (6). The frequent and sometimes unwarranted use of broad-spectrum antibiotics, particularly in hospitalized children, has created an environment conducive to the emergence of resistant pathogens (7).

The increased risk of secondary bacterial infections in children who have recovered from COVID-19 is another important aspect of this study. The most commonly identified pathogens in pediatric COVID-19 cases with secondary bacterial infections were **Klebsiella pneumoniae**, **Escherichia coli**, **Pseudomonas aeruginosa**, and **Staphylococcus aureus**, all of which are known to exhibit varying degrees of resistance (8). **Klebsiella pneumoniae** and **Pseudomonas aeruginosa**, in particular, demonstrated higher resistance rates, with resistance to commonly used antibiotics such as fluoroquinolones, carbapenems, and third-generation cephalosporins (9). These resistance patterns raise significant concerns about the effectiveness of current treatment regimens, as infections caused by these resistant strains may require alternative, more expensive, and often less effective therapies (10).

Geographic variation in antibiotic resistance is a critical finding from this meta-analysis. Studies conducted in low- and middle-income countries showed higher rates of resistance compared to high-income nations (11). This discrepancy likely reflects differences in healthcare infrastructure, diagnostic capabilities, and antibiotic stewardship programs. In many low-resource settings, the lack of access to rapid diagnostic tools means that antibiotics are often prescribed empirically, leading to overuse and the potential for resistance development (12). Additionally, limited access to healthcare resources and essential antibiotics may result in suboptimal treatment regimens, which further contribute to the emergence of resistant strains (13).

In contrast, high-income countries, where healthcare systems are generally better equipped and diagnostic capabilities are more advanced, tend to report lower rates of resistance. However, even in these settings, there are concerns about the overuse of antibiotics, especially in cases where bacterial co-infections are not confirmed but antibiotics are prescribed as a precautionary measure (14). While the prevalence of resistance is generally lower in high-income countries, this analysis highlights that the problem is not unique to resource-limited areas but is a global issue that demands attention (15).

One of the more striking findings of this study is the significant impact of antibiotic resistance on clinical outcomes in pediatric patients (16). The presence of resistant infections was associated with longer hospital stays, higher mortality rates, and poorer overall outcomes. Children with antibiotic-resistant infections spent an average of 18 days in the hospital, compared to 11 days for those with non-resistant infections (17). The increased duration of hospitalization not only places a strain on healthcare resources but also exposes patients to additional risks, such as hospital-acquired infections, further complicating their recovery (18). Mortality rates were also higher in the group with antibiotic-resistant infections, with a mortality rate of 6.5%, compared to 2.1% in those with non-resistant infections. These findings underscore the significant burden that antibiotic resistance places on both the healthcare system and patient health (19).

Given these findings, antibiotic stewardship emerges as a key strategy in combatting antibiotic resistance. Antibiotic stewardship programs, which promote the appropriate use of antibiotics, are essential in reducing unnecessary prescriptions and improving patient outcomes (20). These programs focus on ensuring that antibiotics are prescribed only when necessary and that the right antibiotics are used at the right doses and for the appropriate duration. In high-income countries, antibiotic stewardship programs have been successful in curbing the rise of resistance and improving clinical outcomes (21). However, in low- and middle-income countries, the implementation of such programs is often hampered by limited resources, lack of infrastructure, and inadequate training of healthcare providers (22).

The global nature of antibiotic resistance means that it is a problem that transcends national borders (23). While high-income countries have made significant strides in controlling antibiotic resistance, the rise of resistant strains in pediatric patients in low- and middle-income countries highlights the need for a coordinated global response (2). Effective surveillance systems, global collaboration in research, and the sharing of data on resistance patterns can help track the evolution of resistance and inform treatment strategies (24). In addition, there is a growing need for investments in diagnostic tools, which can help clinicians rapidly differentiate between bacterial and viral infections, reducing the unnecessary use of antibiotics (25).

Furthermore, the overprescription of antibiotics in pediatric COVID-19 cases is compounded by gaps in knowledge and awareness among both healthcare providers and the general public. In many cases, parents may pressure healthcare providers to prescribe antibiotics, believing that antibiotics are necessary for the treatment of viral infections (26). This, coupled with the uncertainty that healthcare providers face in diagnosing bacterial infections during the acute phase of COVID-19, contributes to the overuse of antibiotics. Education campaigns aimed at both healthcare providers and the general public are essential to address these misconceptions and encourage more responsible antibiotic use (27).

The rising prevalence of antibiotic resistance in pediatric populations post-COVID-19 is not just a clinical issue; it is a public health crisis that requires urgent attention (28). The long-term consequences of antibiotic resistance are profound, as infections caused by resistant pathogens become more difficult to treat, leading to higher healthcare costs, prolonged illness, and increased mortality (29). It is essential to take a comprehensive approach to addressing this issue, which includes the judicious use of antibiotics, the promotion of antibiotic stewardship, and the development of new antibiotics and alternative therapies.

In addition to combating antibiotic resistance, there is a need for further research to understand the mechanisms behind resistance in pediatric populations and to identify novel approaches to prevention and treatmen (30). The ongoing surveillance of antibiotic resistance patterns, along with the development of more effective diagnostic tools and vaccines, will be key to managing the evolving landscape of infectious diseases (31). Given the increasing burden of antibiotic resistance, there is a pressing need for concerted global efforts to tackle this problem and mitigate its impact on pediatric health, particularly in the wake of the COVID-19 pandemic.

Conclusion

This meta-analysis has highlighted a concerning increase in antibiotic resistance among pediatric populations following COVID-19 infection. The misuse of antibiotics, particularly in the absence of bacterial co-infections, has contributed to the rise in resistance. The regional variations observed underscore the need for tailored antibiotic stewardship programs, better diagnostic tools, and improved healthcare infrastructure, particularly in low- and middle-income countries. Ultimately, addressing antibiotic resistance requires a global, multi-faceted approach that includes reducing unnecessary antibiotic use, improving diagnostic capabilities, enhancing surveillance, and investing in new treatment options. As the world continues to navigate the aftermath of the COVID-19 pandemic, the need for effective strategies to combat antibiotic resistance has never been more urgent.

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