

## Antibiotics in Children with Pneumonia: a Review

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### ABSTRACT

Pneumonia is one of the most common infections in children; at the same time, it's also a case that consumes lots of days in hospitals with antibiotics. Essentially, antibiotics are medicines that specifically combat infection produced by bacteria, turning out to be some of the important discoveries in the entire history of medicine. This review aims to analyze the types of sensitive and resistant antibiotics in the management of pneumonia in children. Antibiotic resistance is one of the most dangerous health hazards facing the global community, which has grave consequences economically. The literature search in this study is adopted from both Google Scholar and PubMed. While on Pubmed, the keyword used includes "pneumonia", "antibiotics", "children", "PICU"; on Google Scholar, the word used is antibiotics, pneumonia, pediatric, and intensive care joined by using "AND" or "OR". The inclusion criteria in this literature search include published literature within less than 10 years, between 2014 and 2024; antibiotic articles on use scheme in the PICU; literatur of pneumonia in pediatric; and study review about bacterial type examinations. Thus, other articles were excluded that did not represent any empirical data regarding the study of antibiotics, or those that focused only on one kind of antibiotic sine the contextualization of its usage design. From the outcome of the review, the following bacteria types have been identified to be present in pneumonia patients: M. pneumoniae, Acinetobacter baumannii, Staphylococcus, Pseudomonas, and K. pneumoniae. Tetracycline and fluoroquinolone groups are effective choices of antibiotic classes. Mycoplasma pneumoniae, a common bacteria in pneumonia patients with CAP, is resistant to macrolides, leading to the recommendation of combination therapy or tetracycline antibiotics. Meropenem, widely used in VAP patients, is now limited and recommended for other types.

## INTRODUCTION

Pneumonia is an infection common in children and contributes more to the use of antibiotics at home. Sick children are compared to others with other conditions. For some big children, the antibiotic spectrum is narrow ( like amoxicillin or ampicillin ) and is recommended for bacterial pneumonia (CAP). However, broader-spectrum antibiotics are often prescribed. To slow antibiotic resistance and improve outcomes, appropriate prescribing is essential. Hospital-based management programs

have proven successful, but there are some issues when implemented in the ICU (Williams et al. 2023 ).

Antibiotics are medications developed to combat bacterial infections. They have been one of the most important medical discoveries of the 20<sup>th</sup> century. It is estimated that since the discovery of penicillin by Alexander Fleming in 1928, antibiotics have enabled many of today's modern medical practices (Uddin et al. 2021). In very sick patients, faster treatment—measured in hours—is associated with better clinical

outcomes, including mortality. Antibiotics are recommended within one hour in patients showing signs of severe sepsis. Before antibiotic therapy, the push for early antibiotic treatment limited the time to complete studies to confirm the diagnosis of pneumonia and the associated microbiology. Many times, while awaiting findings, broad-spectrum empiric therapy had to be initiated (Lim 2022).

Antibiotics have revolutionized medicine today. They are essential in the treatment of infectious diseases and enable important therapies and procedures. However, these successes hinder their long-term use in the 21<sup>st</sup> century due to two orthogonal problems. The first is that the microbes these drugs target are becoming resistant to them over time. The second is that antibiotic discovery and development is no longer cost-effective because traditional reimbursement models are no longer effective (Cook and Wright 2022).

Some of the major factors contributing to the rise in the number of bacterial species with multidrug resistance include increased antibiotic consumption, misuse and/or abuse, and human travel. Recent reports showed that the increase in the number of antibiotic-resistant microorganisms was inversely proportional to the number of effective antibiotics; no new antimicrobial agents have recently been discovered (Baran, Kwiatkowska, and Potocki 2023). The WHO has acknowledged the rise in antibiotic resistance, coupled with a rise in the number of multidrug-resistant microbes, as a threat to human health. Recent data show that the number of antibiotic-resistant microorganisms is negatively correlated with the number of effective antibiotics. It is estimated that ten million people will die from infections caused by antibiotic-resistant bacteria by 2050 (Pulingam et al. 2022).

The study showed estimated mortality data in patients with ampicillin resistance of 18.8% of 87 patients. Mortality was significantly higher in patients with MDRO (32.4%) than in patients

without MDRO (3.9%). Patients who died including 85.7% of patients with MDRO had significantly longer admission duration, more cultures, and used more antibiotics than patients who survived (Saeedi et al. 2024).

Appropriate use of antibiotics can reduce mortality. In previous studies, several risk factors that can increase mortality are infectious diseases and antibiotic use. Other studies in the hospital environment have found that longer hospital stays, steroid use, impaired renal function, immunodeficiency or neutropenia, use of indwelling urinary catheterization, Infections are a common risk for increased exposure to antibiotics such as vancomycin and 3rd generation cephalosporins. However, patients in the Intensive Care Unit (ICU) who are critically ill and do not have many treatment options are very susceptible to infection (Bhatti et al. 2023). This review aims to discuss antibiotics in the treatment of pneumonia in children and provide an overview of the types of antibiotics that are sensitive and resistant in cases of childhood pneumonia. In addition, this article aims to describe the control of antibiotic resistance in children and improve compliance and selection of antibiotics according to the results of supporting and clinical examinations of patients.

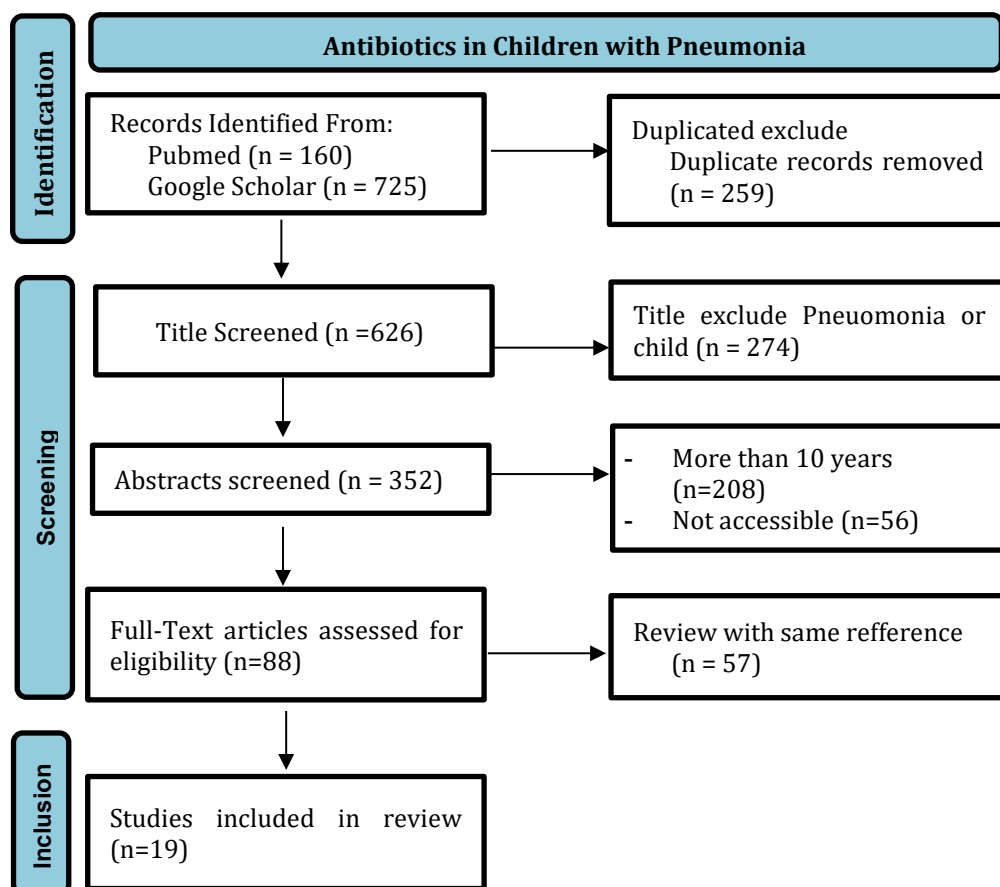
## METHODS

A literature search was conducted using keywords on pubmed and google scholar search engines. The inclusion criteria in this literature search include literature published within less than 10 years, between 2014 and 2024; antibiotic articles on use scheme in the PICU; literature of pneumonia in pediatric; and study review on bacterial type examinations. In addition to the inclusion criteria, researchers also determined the exclusion criteria, namely articles on prophylactic antibiotics, articles that did not get full access, review articles that had the same references. The results of the literature search based on keywords are presented in **Table 1**.

**Table 1. Keyword**

Keywords	Pubmed	Google Scholar
antibiotics, pneumonia, child, trigger	113	281
antibiotics, pneumonia, child, resistance, trigger	46	121
antibiotics, pneumonia, child, trigger, Indonesia	1	210
antibiotics, pneumonia, child, resistant, trigger, Indonesia	0	113

The results of the literature search in table. 1 were then screened using a prism diagram. The screening results with a prism diagram are as in **Figure 1**.



**Figure 1: Prism diagram**

## RESULT AND DISCUSSION

The use of antibiotics in childhood pneumonia shows quite wide variations depending on the type of pathogen, geographic region, and clinical approach used. From the summary results of various studies, *Mycoplasma pneumoniae* is one of the most frequently found pathogens, especially in cases of community-acquired pneumonia (CAP). Studies from several Asian countries such as China, Korea, and Japan show that the macrolide antibiotic group is increasingly losing its effectiveness against *M. pneumoniae* as a result of increased drug resistance (Akashi et al., 2018; Lee et al., 2017; Zhou et al., 2021; Xu & Fang, 2023; Tsai et al., 2021). This has triggered the utilization of alternatives such as tetracycline (e.g., doxycycline and minocycline) and fluoroquinolone (Kim et al., 2017; Wang et al., 2024), although their

application in children is still subject to consideration of risk vs. benefit. Resistance to macrolides, especially to azithromycin, is the most challenging thing in empirical therapy (Hon et al., 2015; Kutty et al., 2019).

Besides *M. pneumoniae*, gram-negative pathogens like *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii* are routinely detected in nosocomial pneumonias like ventilator-associated pneumonia (VAP) and hospital-acquired pneumonia (HAP). These pathogens have high levels of resistance to first-line antibiotics such as beta-lactams, cephalosporins, even carbapenems (Fan et al., 2024; Fu et al., 2022; Aygun et al., 2019; Wong et al., 2024; Wattal & Goel, 2020). China and Turkey studies show that antibiotics such as tigecycline, amikacin, and polymyxin are

effective against these bacteria (Zhang et al., 2021; Ergul et al., 2017).

This review covers several geographic regions and shows differences in empirical therapy policies and antibiotic resistance strengths. So far in Asian countries such as China and Korea, resistance to macrolides and beta-lactams is relatively high (Lee et al., 2017; Zhou et al., 2021), but in Europe and America, treatment strategies are more

diverse based on local levels of resistance occurrence. Russian and European surveys show that *Staphylococcus aureus* and MRSA remain significant pathogens with sensitivity to vancomycin and tigecycline, but display high resistance to methicillin and carbapenems (Khokhlova et al., 2015; Walter et al., 2018; Zhao et al., 2019).

**Table 2. Article Review**

Author (Year)	Location, Research Place	Research Subject, Diagnosis	Research methods	Types of Bacteria	Antibiotic Sensitive	Antibiotic Resistance
(Wong et al., 2024)	Asia TRIGGER	Child, VAP	Retrospective Cohort Study	<i>Staphylococcus, Pseudomonas</i>	second generation cephalosporins and carbapenems	macrolide
(Kutty et al., 2019)	Tennessee, America Hospital Ward	Child, STAMP	Prospective Cohort Study	<i>Mycoplasma pneumoniae</i>	fluoroquinolones (eg, levofloxacin and moxifloxacin), and doxycycline	Macrolides
(Zhou et al., 2021)	Shanghai, China Hospital Ward	Child, CAP	Retrospective Cohort Study	<i>Mycoplasma pneumoniae</i>	fluoroquinolone	azithromycin and the macrolide group
(Hon et al., 2015)	China and Hong Kong Hospital Ward	Child, VAP	Case Report	<i>Mycoplasma pneumoniae</i>	tetracycline or fluoroquinolone	macrolide
(Zhang et al., 2021)	China	Child, VAP	Clinical Trial	<i>Acinetobacter baumannii</i>	aminoglycosides (eg, amikacin), sulfonamides (eg, sulfamethoxazole compounds), and tetracyclines (eg, tigecycline)	cefepime, ceftazidime, ampicillin, ampicillin sulbactam, piperacillin tazobactam, ampicillin
(Fan et al., 2024)	China TRIGGER	Child, HAP STAMP	Retrospective Cohort Study	<i>Klebsiella pneumoniae</i>	polymyxin and tigecycline	meropenem and imipenem
(Fu et al., 2022)	China Hospital Ward	Child, HAP STAMP	Clinical Trial	<i>Klebsiella pneumoniae</i>	amikacin, tigecycline, and polymyxin B, colistin	Ertapenem, imipenem and meropenem
(Aygün et al., 2019)	Istanbul, Türkiye Hospital Ward	Child, HAP STAMP	Clinical Trial	<i>Pseudomonas aeruginosa</i>		beta-lactams, quinolones, and aminoglycosides
(Wang et al., 2024)	China Hospital Ward	Child, CAP	Reviews	<i>M. pneumoniae</i>	tetracyclines and quinolones	macrolide antibiotics.

**Table 2. Continue**

Author (Year)	Location, Research Place	Research Subject, Diagnosis	Research methods	Types of Bacteria	Antibiotic Sensitive	Antibiotic Resistance
(Xu and Fang, 2023)	China Hospital Ward	Child, CAP	Case Report	<i>M. pneumoniae</i>	omadacycline	Azithromycin

(Ergul et al., 2017)	Türkiye Hospital Ward	Child, VAP	Retrospective Cohort Study	<i>Klebsiella pneumoniae</i> , <i>Pseudomonas aeruginosa</i> , and <i>Acinetobacter baumannii</i>	amikacin, tigecycline	Amikacin and meropenem
(Wattall & Goel, 2020)	India TRIGGER	Child, VAP	Reviews	<i>Klebsiella pneumoniae</i>	Ceftriaxone	ampicillin cefotaxime piperacillin-tazobactam and levofloxacin
(Tsai et al., 2021)	Taiwan Hospital Ward	Child, CAP	Reviews	<i>M. pneumoniae</i>	Tetracycline (doxycycline or minocycline) or fluoroquinolone	Macrolides (azithromycin, clarithromycin, erythromycin)
(Akashi et al., 2018)	Japan Hospital Ward	Child, CAP	Retrospective Cohort Study	<i>M. pneumoniae</i>	Tetracycline	Macrolides
(Lee et al., 2017)	Korea Hospital Ward	Child, CAP	Retrospective Cohort Study	<i>M. pneumoniae</i>	tetracycline or fluoroquinolone	Macrolides
(Kim et al., 2017)	Korea Hospital Ward	Child, STAMP	Clinical Trial	<i>M. pneumoniae</i>	Doxycycline, quinolone,	Macrolides
(Zhao et al., 2019)	China Hospital Ward	Children, HAP, and CAP	Clinical Trial	<i>Streptococcus pneumoniae</i>	linezolid, moxifloxacin, and vancomycin	erythromycin and clindamycin
(Khokhlova et al., 2015)	Russia Hospital Ward	Children, HAP, and CAP	Clinical Trial	<i>S. aureus</i> and MRSA	vancomycin	Methicillin
(Walter et al., 2018)	Europe Hospital Ward	Child, HAP	Retrospective cross-sectional	<i>Staphylococcus aureus</i> , <i>Pseudomonas aeruginosa</i> , <i>Klebsiella spp.</i>	Vancomycin, amikacin, tigecycline	Methicillin, carbapenem

The results of the literature review have quite wide variations seen from the location of the study, type of pneumonia, method, and type of sensitive and resistant antibiotics (**Table 2**). Treatment inpatient room and care unit intensive. Based on location, most research is carried out in the Asian region with several different countries. Variations of pneumonia include categories of community-acquired pneumonia (CAP), hospital-acquired pneumonia (HAP), and ventilator-acquired pneumonia (VAP) (Reyes et al., 2024).

### Bacterial Patterns in Pneumonia

Bacteria are pathogens that can cause infections in humans and other living things (Bartlett et al. 2022). Bacteria that infect patients with pneumonia are *M. pneumoniae*, *Acinetobacter baumannii*, *Staphylococcus*, *Pseudomonas*, and *K. pneumoniae* (Wong et al. 2024) (Wattal and Goel. 2020). The most common type of pneumonia is *M. pneumoniae* (Kim et al. 2017). *Staphylococcus aureus*,

*Pseudomonas aeruginosa*, and *Klebsiella spp* bacteria are often found in patients with HAP-type pneumonia (Walter et al. 2018). Meanwhile, patients with VAP type are caused by bacteria such as *Pseudomonas aeruginosa*, *K. pneumoniae*, and *Acinetobacter baumannii* (Zhang et al. 2021) (Ergul et al. 2017). Based on this literature study, countries or regions tend to have the same types of bacteria. Pneumonia-causing bacteria found in Asian regions such as Korea, China, India, Hong Kong, and Turkey are no different from bacteria found in European regions such as Russia.

### Type of antibiotic used

The choice of antibiotics in pneumonia patients can be categorized based on severity. Patients with low severity can be treated with cotrimoxazole and a normal dose of amoxicillin. Research in Pakistan shows that cotrimoxazole therapy combined with injectable penicillin can provide better patient recovery compared to high dose oral amoxicillin given for 5-7 days (Tramper-Stranders 2018). Clinical research



was conducted by testing several patients with different conditions. García Romero et al. 2024 in his research explained related to the administration of Ceftazidime therapy with avibactam in pediatric intensive care unit (PICU) patients. The study showed that the administration of Ceftazidime therapy with avibactam can be used for short-term empirical treatment in patients who have previous bacterial colonization (García Romero et al. 2024).

Based on the type of pneumonia, several antibiotics are still sensitive in the treatment of pneumonia. CAP pneumonia with the type of *M. pneumoniae* bacteria is sensitive to tetracycline antibiotics such as Doxycycline and Quinolone (Kim et al. 2017) (Lee et al. 2017). VAP pneumonia patients with the type of *Acinetobacter baumannii* bacteria are sensitive to aminoglycoside antibiotics (eg, amikacin), sulfonamides (eg, sulfamethoxazole compounds), and tetracyclines (eg, tigecycline) (Zhang et al. 2021) (Ergul et al. 2017). Meanwhile, patients with HAP and the types of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *MRSA* and *Klebsiella spp* bacteria can be treated with vancomycin and tigecycline (Khokhlova et al. 2015) (Walter et al. 2018).

Other antibiotics that are still active and can be used in the administration of HAP and CAP therapy are linezolid and moxifloxacin with the type of bacteria that infects, namely *Streptococcus pneumoniae* (Zhao et al. 2019).

### Resistance Antibiotics

The height-resistance antibiotics to general drugs include the following: ampicillin 90.70%-94.9%, cefotaxime 71.4%-92.4%, piperacillin tazobactam 27.5%-31.2%, and levofloxacin 39.8%-42.4%. Resistance to carbapenems, especially because of the blaNDM gene, is found in all center studies with level variability of 1%-79%, especially in *Klebsiella pneumoniae* and *Acinetobacter baumannii* (Wattal and Goel 2020). *Streptococcus pneumoniae* resistance to clindamycin, erythromycin, and tetracycline, as well as *Staphylococcus aureus* against tetracycline, indicating a decline significant. Resistance of *Klesiella pneumoniae* to amoxicillin/acid clauvanate (AMC) and trimethoprim/sulfamethoxazole (SXT), as well as *Acinetobacter baumannii* against cefotaxime

and SXT, also decreased in a way significant (C. Fan et al. 2024).

*Mycoplasma pneumoniae* is one of the microorganisms that often appear in patients children under the age of 6 years. *Mycoplasma pneumoniae* is found in pneumonia patients with CAP. The bacteria has stated resistance to the given patient therapy macrolide as much as 90.2%. However, resistance to the No causes a high mortality rate, where the number mortality is Still low with a value of 3.9% of infected patients (Zhou et al. 2021).

Methicillin and carbapenem antibiotics are used for treatment in HAP patients has experience resistance if the patient is infected with *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Klebsiella bacteria spp* (Walter et al. 2018). Meanwhile, the antibiotics erythromycin and clindamycin are resistant to HAP and CAP patients infected with *Streptococcus pneumoniae* bacteria (Zhao et al. 2019).

The bacteria *Acinetobacter baumannii* in pneumonia patients with VAP has been claimed to be resistant to the following antibiotics: cefepime, ceftazidime, ampicillin, ampicillin-sulbactam, piperacillin-tazobactam, and ampicillin. (Zhang et al. 2021). Another study conducted on VAP patients with the types of bacterium *Pseumonomas aeruginosa*, *Klebsiella pneumoniae*, and *Acinetobacter baumannii* in Turkey showed a level of resistance to the antibiotics amikacin and meropenem (Ergul et al. 2017).

### CONCLUSIONS

*Mycoplasma pneumoniae* is a bacteria that is often found in pneumonia patients with CAP and has been claimed to be resistant to macrolides. Antibiotics that are widely used in PICU with CAP are macrolides, but with increasing resistance, the use of combination therapy or tetracycline antibiotics is more recommended and can reduce fever in patients as an early sign of infection. Meropenem is an antibiotic that is widely used in patients with VAP but has experienced resistance, so its use is starting to be limited and recommended for other types according to the bacteria that infect the patient.

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### AUTHORS' CONTRIBUTIONS

First author creating ideas, conducting data analysis, and writing draft article. Second author provide guidance and direction, provide feedback, and approve before publication.

### CONFLICT OF INTERESTS

In creating this scientific work, i as the author hope that the use of antibiotics in hospitals, especially for pneumonia, can be applied by applicable antibiotic guidelines and established culture results.

### ETHICAL CONSIDERATION

I have fully complied with the ethical issues in writing this scientific paper, including avoiding plagiarism and ensuring the originality of every idea conveyed. In addition, I as the author do not guarantee that all data used are valid and accountable. I also ensure that this work is not published in duplicate elsewhere.

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