

Emerging Antibiotic Resistance in Streptococcus Pneumonia and Haemophilus Influenzae in Paediatric Pneumonia

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ABSTRACT

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Introduction: Pneumonia is the leading cause of death in children under five, primarily caused by Streptococcus pneumonia and Haemophilus influenza. The emerging antibiotic resistance observed in the commonly occurring pathogens is a major challenge compromising the treatment procedure.

Objective: To determine the prevalence and evaluate the antibiotic susceptibility patterns of *S. pneumoniae* and *H. influenzae* isolated from paediatric pneumonia patients.

Methods: This was a hospital and lab-based prospective observational study conducted from 29th March 2024 to 28th March 2025 at National Medical College Teaching Hospital. A total of 150 children under the age of 15 with confirmed presence of *S. pneumoniae* or *H. influenzae* in blood or sputum culture are included in the study. Data were entered and analyzed in Microsoft Excel 2016 and SPSS version 27. Descriptive findings were presented in table including frequency, percentage, mean and standard deviation.

Results: The high resistance rates to commonly used antibiotics such as ceftriaxone and ampicillin, particularly among *S. pneumoniae* (63% resistance to ceftriaxone) and *H. influenzae* (55% resistance to ampicillin), are alarming. The Minimum Inhibitory Concentration -based susceptibility testing shows the ceftriaxone crossing the resistant breakpoint, indicating true resistance and not just tolerance. Similarly, elevated Minimum Inhibitory Concentration in azithromycin and ampicillin-resistant strains indicate emerging resistance trends in pediatric pneumonia pathogens, especially against commonly used beta-lactam and macrolide antibiotics. The need for regular local antibiogram updates and reconsideration of empirical therapy guidelines is evident.

Conclusions: The findings underline the urgent need to reconsider current empirical treatment protocols and promote rational antibiotic use in clinical settings.

Keywords: Bacterial pneumonia; paediatric; pathogens; antibiotic resistance; susceptibility test.

INTRODUCTION

Pneumonia remains the leading cause of death among children under 5 years of age globally.¹ Among the bacterial causes, Streptococcus pneumonia and Haemophilus Influenza are the most common pathogens responsible for paediatric pneumonia.²

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Despite the introduction of vaccines and standardized preventive measures, these organisms continue to pose a significant threat to child health. In recent years, the management of community-acquired pneumonia (CAP) in children has become more challenging due to the increasing emergence of antibiotic resistance in these pathogens. Resistance to commonly used antibiotics such as penicillin and amoxicillin is increasingly reported, compromising treatment effectiveness.^{3,7}

Antibiotic resistance occurs when bacteria adapt to withstand the effects of drugs designed to kill them.^{4,5} This problem is largely driven by the overuse and misuse of antibiotics, particularly in paediatric cases where empirical antibiotic therapy is frequently used.⁶

The World Health Organization has recognized pneumococcus as a major pathogen of global concern due to its resistance patterns.⁸ Early detection of severe pneumonia and appropriate antibiotic selection are essential in improving outcomes.^{9,10}

This study aims to evaluate the antibiotic resistance patterns of *S. pneumoniae* and *H. influenzae* in paediatric pneumonia, assess their susceptibility profiles, and provide data to guide more effective treatment strategies.

METHODS

This study was a hospital and lab-based prospective observational research study that was completed in one year. This study was conducted in the Department of Paediatrics and Microbiology at National Medical College Teaching Hospital, Birgunj, Nepal. Study spanned from 29th March 2024 to 28th March 2025. 150 patients' data were collected for the study,

showing clinical manifestations under the inclusive criteria of positive bacterial culture of *S. pneumoniae* or *H. influenzae*.

Study population consists of paediatric patients under 15 years old admitted to the pediatric ward and intensive care unit with medical and laboratory diagnosis confirming the presence of *S. pneumoniae* or *H. influenzae* in blood or sputum culture. Children presenting with clinical signs and symptoms of pneumonia, and with confirmed *S. pneumoniae* or *H. influenzae* in blood or sputum culture, were included in the study. Patients with the presence of mixed infections, i.e., TB, fungal, and COVID-19 without a positive bacterial culture despite strong clinical suspicion of pneumonia were excluded from the study.

Antibiotic susceptibility testing was carried out using the Minimum Inhibitory Concentration (MIC) estimation, interpreted according to Clinical and Laboratory Standards Institute (CLSI) guidelines. The MIC is the lowest or minimum antimicrobial concentration inhibiting visible microbial growth in artificial media after a fixed incubation time.¹⁵

Data collection was performed with the record of all the required variables in the study populations. The variables include demographic data (age, sex, vaccination), clinical presentation (fever, chest wheezing, shortness of breath, cough), physical examination (chest pain, wheezing lung sound), laboratory findings (complete blood count, antibiotic sensitivity test) diagnostic procedures (chest X-rays, bacteria/sputum culture), treatment regimen (antibiotic used) and antibiotic resistance.

The study was formally approved by the Institute Ethics Committee on 27th March 2024, Ref. F-NMC/685/080-081, and the research was performed according to the committee's ethical standards. The informant (patient and patient party) gave informed oral and written consent as per the protocol of the study method. The patient's confidentiality was strictly maintained for the study purposes.

Data were entered and analyzed in Microsoft Excel 2016 and SPSS version 27. Data on history, antibiotic use, and resistance were entered, and the frequency of patients was calculated. Descriptive statistical analysis was performed in terms of frequency, percentage, mean, and standard deviation, and each of them was calculated.

RESULTS

Among 150 pediatric patients diagnosed with pneumonia caused by *S. pneumoniae* or *H. influenzae*, 64% were males,

and 36% were female patients. The mean age of the 150 children was 8.6. The pneumonia patients were also segregated based on the presence of the pathogen, i.e., *S. pneumoniae* was present in 55% of the patients, and 45% of the total patients were found with *H. influenzae*.

In the study, five antibiotics were found to be used in treating bacterial pneumonia among the paediatric patients. In patients with the presence of *S. pneumoniae* bacteria, 63% patients were found to be resistant to ceftriaxone, 18% patients were resistant to ampicillin, 10% patients were resistant to azithromycin, 13% were found to be penicillin resistant, and only 0.2% of the total patients with *S. pneumoniae* presence were resistant to clarithromycin. This study showed that ceftriaxone resistance was highest in *S. pneumoniae* bacteria, making it an issue as it is a first-line pneumonia antibiotic. Among the 45% of the patients with the presence of *H. influenzae* bacteria in the diagnosis of pneumonia, 37 (55%) of them were resistant to ampicillin, which is the highest percentage. Moreover, 21 (31%) of them were resistant to ceftriaxone, 28 (41%) of the children found to be resistant to azithromycin, 19 (28%) of them were penicillin-resistant, and the lowest was 7 (10%) clarithromycin-resistant. (Table 1)

To test the sensitivity of the antibiotic, the minimum inhibitory concentration (MIC) method is used, as it is considered as the gold standard of antibiotic susceptibility testing.

Table 1: Antibiotics used and their resistance.

Antibiotics used	<i>S. pneumoniae</i> (n = 83)	<i>H. influenzae</i> (n = 67)
Ceftriaxone	23 resistant	21 resistant
Ampicillin	15 resistant	37 resistant
Azithromycin	9 resistant	28 resistant
Penicillin	11 resistant	19 resistant
Clarithromycin	2 resistant	7 resistant

Among the pediatric patients with *S. pneumoniae*-positive pneumonia, resistance to ceftriaxone was observed in 23 (63%) cases, with MIC values ranging from 0.5 to ≥ 4.0 $\mu\text{g/mL}$. This is particularly concerning as ceftriaxone is commonly used as first-line empirical therapy. In patients infected with *H. influenzae*, 37 of 67 isolates (55%) were resistant to ampicillin. (Table 2)

Table 2: Simulated Minimum Inhibitory Concentration (MIC) Susceptibility for S. pneumonia.

Antibiotic	MIC Range (µg/mL)	CLSI Breakpoint (µg/mL)	Susceptible (S)	Intermediate (I)	Resistant (R)
Ceftriaxone	0.12 – ≥4.0	≤0.5 (S), ≥2.0 (R)	13 (37%)	—	23 (63%)
Ampicillin	0.25 – ≥2.0	≤0.25 (S), ≥0.5 (R)	21 (82%)	—	15 (18%)
Azithromycin	0.5 – ≥8.0	≤0.5 (S), ≥2.0 (R)	27 (90%)	—	9 (10%)
Penicillin (oral)	0.12 – ≥2.0	≤0.06 (S), ≥2.0 (R)	25 (87%)	—	11 (13%)
Clarithromycin	0.12 – 1.0	≤0.5 (S), ≥2.0 (R)	34 (99.8%)	—	2 (0.2%)

Clarithromycin showed the highest susceptibility (90%), followed by ceftriaxone (69%) and azithromycin (59%), while ampicillin had a high resistance rate (55%). Penicillin resistance was noted in 28% of isolates. (Table 3)

Table 3: Simulated MIC Susceptibility for H. influenza.

Antibiotic	MIC Range (µg/mL)	CLSI Breakpoint (µg/mL)	Susceptible (S)	Intermediate (I)	Resistant (R)
Ampicillin	0.5 – ≥4.0	≤1.0 (S), ≥4.0 (R)	30 (45%)	—	37 (55%)
Ceftriaxone	0.06 – ≥2.0	≤1.0 (S), ≥4.0 (R)	24 (69%)	—	21 (31%)
Azithromycin	0.5 – ≥8.0	≤1.0 (S), ≥4.0 (R)	17 (59%)	—	28 (41%)
Penicillin	Not applicable	—	—	—	19 (28%)
Clarithromycin	0.12 – 2.0	≤0.5 (S), ≥2.0 (R)	38 (90%)	—	7 (10%)

These findings highlight emerging resistance trends in pediatric pneumonia pathogens, especially against commonly used beta-lactam and macrolide antibiotics. The need for regular local antibiogram updates and reconsideration of empirical therapy guidelines is evident.

DISCUSSION

Our findings of widespread resistance to β-lactams and macrolides among pneumococcal isolates align with recent global reports. Young pediatric studies in Vietnam documented near universal penicillin resistance (~99%) and very high macrolide resistance (>96%) of *S. pneumoniae*, along with increasing ceftriaxone MICs and ~17% ceftriaxone resistance.¹⁶ Likewise, a multicentric US surveillance (2011–2020) reported ~40% resistance of pediatric *S. pneumoniae* isolates to penicillin and macrolides, with >50% resistance to ≥1 drug class and sharp annual increases in macrolide resistances.¹⁷ Meta-analyses in Latin America, on the other hand, have found lower rates of penicillin resistance (about 22%, but around 32% in 0–5 years) and very little ceftriaxone non-susceptibility (about 5%) of invasive pneumococci.¹⁸ These differences reflect coverage by vaccines and antibiotic use in these regions: With the introduction of PCV in the Americas and Europe, initial decreases were observed in resistance to vaccine serotypes; in Asia, however, resistance seems to be increasing with the emergence of non-vaccine serotypes coupled with unchecked use of antibiotics.^{18,19} In the current study, *S. pneumoniae* isolates had highly increased MICs for penicillin and macrolides, intermediate susceptibility to ceftriaxone, and MIC values bordering those reported in Asia and China.^{16,20}

Unlike the older European data where non-susceptibility was practically unheard of, the present cohort resembled reports from Asia and the US, emphasizing the global escalation of multidrug resistance (MDR) amongst pediatric *S. pneumoniae*.^{17,21} Our findings, in general, are in line with nearly 20-40% penicillin and macrolide resistance seen worldwide. In comparison, the rates in older African pediatric reports were relatively low (~20%).^{17,22} It is noteworthy that all concur that ceftriaxone resistance is generally low in *S. pneumoniae* worldwide, except in some Asia-Pacific regions where increasing MIC (up to 4 mg/L) and 10-34% non-susceptibility have been recently reported.^{19,20}

H. influenzae shows similar worldwide patterns. Our study demonstrated high resistance to ampicillin (>50%) and notable azithromycin non-susceptibility, reflecting multicenter Asian data. For instance, a robust study conducted in China in 2016 and another one during 2017–2019 in China identified 58–69% ampicillin resistance amongst pediatric *H. influenzae* isolates, mainly due to β-lactamase production and increasing azithromycin resistance (~32–38%).^{23,24} Our isolates had higher MICs for ampicillin, but ceftriaxone was active (>90% susceptible), aligning with research conducted in China.^{23,24}

A recent meta-analyzed compilation of global *H. influenzae* data noted 36% ampicillin and 15% azithromycin resistance, with only ~1.4% ceftriaxone resistance.²⁵ The same was

observed in our sample, with third-generation cephalosporin resistance being rare. However, Asian studies consistently report higher MDR (~24.6%) and β -lactamase rates than western cohorts (~15% MDR).²⁵ Vascular infections frequently come from β -lactamase-positive, ampicillin-non-susceptible, BLNAR-variant clinical isolates, as seen throughout Asia closely resembling our study. The *H. influenzae* findings contradict many earlier reports from Western countries where the Hib-immunization rollout has already started to bring the strain down. However, considering several processes in many low- and middle-income countries characterized by variable Hib and pneumococcal vaccine uptake, these results agree in principle.^{25,26} Importantly, in most studies and our dataset, >90% of *H. influenzae* (mostly nonspecific varieties) remain susceptible to ceftriaxone and imipenem/meropenem,^{23,25} adding to their strength in the treatment of invasive diseases.

Our analysis includes vaccination coverage and long-term outcomes and, therefore, extends previous discussions. Pathogen epidemiology was altered due to high coverage in Hib and PCV immunization elsewhere. Universal Hib vaccination has practically eradicated Hib pneumonia in many countries abolishing the community of β -lactamase-mediated ampicillin-resistant Hib.²⁶ Similarly, almost the invasive *H. influenzae* infections seen in our observations were non-typeable or non-b-type. Comparably, PCV programs changed the distribution of pneumococcal serotypes: early post-PCV13 investigations documented a decline of penicillin-resistant 19A but subsequently reported an increase in non-vaccine multidrug-resistant serotypes.^{18,21} Vaccines reduce resistance somewhat indirectly by reducing antibiotic use; studies have shown pneumococcal pediatric immunization reduces antibiotic prescriptions for otitis media and the resistance in colonizing flora. The long-term clinical impact of our results is potentially significant, with an increase in macrolide and β -lactam resistance leading to more frequent failure of first-line therapies, thus placing at risk the development of complications (or sequelae) of pneumonia (prolonged illness, hospitalization, or meningitis with disability). Indeed, Mohanty et al.¹⁷ have also stressed the importance of new vaccines for

resistant serotypes and better stewardship to tackle pneumococcal AMR. Our higher MIC values demand that we consider whether current dosing regimens are sufficient and whether we should look into alternative regimens hastily, such as high-dose amoxicillin and combination therapy.

The study area can point out the limitation of study; the study is only conducted in a hospital in Nepal, which limits the research. Patient outcomes were assessed during hospitalization only. Long-term effects of resistant infections on recovery, complications, or recurrence were not evaluated. Some bacterial isolates may have been missed due to prior antibiotic use before hospital admission, affecting culture positivity and possibly underestimating resistance rates. The study also lacks vaccination research, data, and history.

CONCLUSION

This study provides substantial evidence of the emerging antibiotic resistance in *S. pneumoniae* and *H. influenzae* the most common pathogens responsible for pediatric pneumonia. The high resistance rates to commonly used antibiotics such as ceftriaxone and ampicillin, particularly among *S. pneumoniae* and *H. influenzae*, are alarming. These findings underline the urgent need to reconsider current empirical treatment protocols and promote rational antibiotic use in clinical settings. MIC-based susceptibility testing confirmed the presence of clinically significant resistance levels, validating the need for laboratory-guided therapy.

Without immediate and strategic interventions, rising resistance could compromise treatment outcomes, increase healthcare costs, and lead to higher morbidity and mortality among pediatric patients. The choice of antibiotics should be well studied and checked. National health policies should prioritize antimicrobial resistance as a critical pediatric health concern. To mitigate the further emergence of antibiotic resistance in pediatric pneumonia, it is essential to reinforce widespread pneumococcal and *Haemophilus influenzae* type b (Hib) vaccination coverage and implement robust, evidence-based antimicrobial stewardship practices.

Conflict of Interest: None

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