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Clinical Spectrum and Antibiotic Resistance Patterns in Upper and Lower Respiratory Tract Infections: A One-Year Observational Study in the Pediatric Population

Salman Ali[1], Asra Ferozi[2] ✉, Uzma Arshad[3], Ayesha Saddique[3], Muhammad Abdullah Islam[4]

[1]Department of ENT, Nishtar Medical University and Hospital, Multan – Pakistan [2]Department of Community Medicine, Times Institute, Multan - Pakistan [3]Department of Community Medicine, Multan Medical and Dental College, Multan – Pakistan [4]Maryam Hospital, Bahawalpur – Pakistan

Corresponding Author:
Asra Ferozi
Department of Community Medicine,
Times Institute,
Multan - Pakistan
Email: asrayusra1695@gmail.com

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ABSTRACT

Background: Respiratory tract infections are a major cause of morbidity in children, with a high burden in low- and middle-income countries like Pakistan. Inappropriate antibiotics use further compounds antimicrobial resistance. Local epidemiological and resistance data are essential to guide empiric therapy and stewardship strategies.

Objective: To evaluate the clinical characteristics, prevalence, and etiological patterns of upper and lower respiratory tract infections in the pediatric population, and to assess the antibiotic resistance profiles of the causative pathogens over a one-year period.

Methodology: We conducted a one-year observational study (January–December 2023) at a tertiary care hospital in Multan, enrolling 1,180 pediatric patients with clinically diagnosed URTIs or LRTIs. Data on demographics, seasonal trends, microbiology, and antibiotic resistance were collected. Microbiological testing followed CLSI guidelines, and antimicrobial susceptibility was assessed by Kirby–Bauer disk diffusion. Statistical analysis was performed using SPSS v26 with $p<0.05$ considered significant.

Results: URTIs accounted for 71.4% of cases, while LRTIs were more frequent in children under five (OR 1.69; 95% CI 1.27–2.24). Culture positivity was higher in LRTIs (78.9%) than URTIs (47.7%, $p<0.001$), with *S. pneumoniae* and *H. influenzae* predominating. Amoxicillin resistance exceeded 50% in major pathogens, azithromycin resistance was moderate, and ceftriaxone retained good activity. Hospitalization was required in 19.1% of patients, predominantly with LRTIs.

Conclusion: Pediatric respiratory infections in Multan show high antibiotic resistance, particularly to amoxicillin, with seasonal peaks in winter and monsoon. Findings underscore the need for locally tailored empiric guidelines, vaccination, and stewardship interventions. Strengthening surveillance can help optimize antimicrobial use and improve child health outcomes.

Keywords: Pediatric Respiratory Infections; Antimicrobial Resistance; Upper Respiratory Tract Infection; Lower Respiratory Tract Infection

Introduction

Respiratory tract infections (RTIs) are among the most common illnesses among children, with lower respiratory tract infections (LRTIs), especially pneumonia which is continuing to be among the leading causes of child deaths around the world. In 2015, an estimated 138 million children under the age of five had pneumonia, resulting in an estimated one million deaths (over 90% of which were in low- and middle-income countries (LMICs), including Pakistan).[1] Pneumonia primarily affects very young children, and is aggravated by malnutrition, overcrowding, and limited vaccination coverage, all common features in resource-poor settings.[1,2]

Pneumonia in Pakistan has been recognized as a public health problem for a long time. There are estimates that between 1% and 4%, or 15 million episodes of illness in total, of acute respiratory infections occur annually in under-five children.[3] Most cases are seen in settings where preventive infrastructure (i.e., the pneumococcal and Hib vaccines) had yet to be fully realized. Pneumonia was also the principal cause of morbidity and mortality in our children admitted to pediatric case medicine or ICU. Case fatality rates in the literature have been reported at or around 14%.[4] The tentative morbidity and mortality figures are alarming and emphasize the need for improved surveillance and management in the pediatric population.

Upper respiratory tract infections (URTIs) are mostly viral and self-limiting and are frequently encountered in primary care and are attributed to many visits; however, there is abundant evidence that antibiotics are prescribed despite absent benefit in these cases. In a recent cross-sectional study from central Punjab, all children admitted to hospital with URTIs received antibiotics, and only about 11% of prescriptions were appropriate based on WHO indicators and pediatric guidelines.[5] The inappropriate prescription of antibiotics extends to lower respiratory tract infections (LRTIs): in a multi-centre review comparing children admitted to hospital under the age of five with LRTIs, over 90% of antibiotics were prescribed inappropriately based on dose, route or indication.[6] This unacceptable level of inappropriate use, compounded by a lack of reliable microbiologic support, is supportive of antimicrobial resistance (AMR) and demonstrates there is a need for tougher stewardship efforts.

Indeed, AMR continues to rise rapidly in pediatric practice across locations in Pakistan. A point prevalence survey among pediatric wards in Punjab showed 82% of inpatients received antibiotics and more than 72% of these were in the WHO's Watch category; importantly, 2% of these prescriptions were based on culture results.[7] More recently a study conducted in a tertiary hospital in Abbottabad also found significant levels of multidrug resistant organisms, including methicillin-resistant Staphylococcus aureus (MRSA), and resistant Gram-negative bacteria in children.[8] This same work demonstrated a need for stewardship, improved diagnostic availability and regular surveillance in pediatric practice.

Complicating the issue more, viral pathogens play an important role in respiratory illness. Data from rural Pakistan suggest that the frequency of viral infections is higher than bacteria in severe pediatric pneumonia. In Sindh, a community-based cohort study found that viral pathogens were identified in 77.8% of swabs from children younger than two years with severe pneumonia, while the supporting bacterial data was limited.[9] These findings highlight the need for coordinated viral and bacterial surveillance to provide an evidence-based approach to targeted therapy.

There is a definite gap in current knowledge: and though the national-level data indicates a gross misuse of antibiotics and resistance in children, there is still a scarcity of locally relevant microbiological and epidemiology studies especially in cities such as Multan. As a step to remedy this, we carried out a one-year observational study involving children with upper and lower respiratory tract infections in Multan. The main goals of the study were to characterize the clinical spectrum of both URTIs and LRTIs in children, as well as to identify the potential bacterial pathogens and their antibiotic resistance patterns. The findings lead to improved, informed decisions for local empiric therapy; enhance antimicrobial stewardship and ultimately improve the health outcomes of children in our region.

Objective

To evaluate the clinical characteristics, prevalence, and etiological patterns of upper and lower respiratory tract infections in the pediatric population, and to assess the antibiotic resistance profiles of the causative pathogens over a one-year period.

Methodology

This was a hospital-based, observational study conducted over a one-year period, from January 2023 to December 2023, at Nishtar Medical University and Hospital, Multan, Pakistan. The hospital is a tertiary care teaching facility serving a mixed urban and peri-urban population, with a dedicated pediatric ward and outpatient clinic.

A total of 1,180 consecutive pediatric patients presenting with respiratory tract infections were included. Patients were recruited from both the outpatient department (OPD) and inpatient pediatric wards. Children aged 1 month to 12 years were eligible, irrespective of sex.

To be eligible for the study, children must have a clinical diagnosis of either an upper or lower respiratory tract infection (URTI or LRTI), confirmed by a pediatrician. Their parents or guardians must also be willing to provide informed consent for participation. However, certain children will not be included in the study. Newborns under one month of age, as well as those with known chronic lung conditions like cystic fibrosis or bronchopulmonary dysplasia, will be excluded. Additionally, children with incomplete medical records or whose parents or guardians choose not to give consent will not participate. This ensures the study focuses on the right group while respecting family decisions and medical histories.

URTIs were defined as infections involving the nasal cavity, pharynx, and/or larynx, including acute pharyngitis, tonsillitis, and otitis media, diagnosed based on history and physical examination. LRTIs included pneumonia and bronchiolitis, diagnosed using clinical signs (tachypnea, lower chest indrawing, auscultatory findings) supported by chest radiographs when indicated, following WHO guidelines for childhood pneumonia classification.

A specialized structured proforma was used to collect demographic data (age, sex), clinical presentation, diagnosis, seasonal distribution of cases, microbiological findings, antibiotic prescription patterns, and outcomes. Data were collected at the point of care by trained pediatric residents and verified by attending pediatricians.

In a subset of patients (n = 615; 52.1% of total), microbiological evaluation was performed. For suspected bacterial infections, appropriate specimens (nasopharyngeal swabs, sputum in older children, or bronchoalveolar lavage in severe cases) were collected under aseptic precautions.

Samples were transported promptly to the hospital microbiology laboratory for culture and sensitivity testing. Standard culture media, including blood agar, chocolate agar, and MacConkey agar, were used according to CLSI guidelines. Identification of isolates was based on colony morphology, Gram staining, and relevant biochemical tests.

Antimicrobial susceptibility testing (AST) was performed using the Kirby–Bauer disk diffusion method on Mueller–Hinton agar, interpreted as per CLSI 2023 breakpoints. The antibiotics tested included amoxicillin, azithromycin, ceftriaxone, levofloxacin, and others based on isolate type. Methicillin resistance in *Staphylococcus aureus* was confirmed using cefoxitin disk testing.

The study focused on three main outcomes. First, it looked at how common upper and lower respiratory tract infections (URTIs and LRTIs) were among the children included. Second, it identified the specific bacteria causing infections in cases where lab cultures came back positive. Third, it examined how resistant these bacteria were to common antibiotics, helping understand which treatments might not work as well.

Beyond these primary goals, the research also explored additional insights. It tracked whether infections were more frequent during certain seasons, which could help predict future outbreaks. The study also recorded how often children needed hospitalization, how long they stayed in the hospital, and whether any deaths occurred during the study period. These findings provide a clearer picture of how severe these infections can be and how they impact children's health.

Data were initially entered into Excell sheet, designed especially for data collection purposes from where all data were shifted into SPSS version 26.0 (IBM Corp., Armonk, NY, USA) for analysis. Continuous variables were summarized as means ± standard deviation (SD) or medians (interquartile range, IQR) depending on normality. Categorical variables were presented as frequencies and percentages.

Comparisons between groups (e.g., URTI vs LRTI, <5 years vs ≥5 years, male vs female) were made using the Chi-square test or Fisher's exact test for categorical variables, and the independent samples t-test or Mann–Whitney U test for continuous variables.

Odds ratios (OR) with 95% confidence intervals (CI) were calculated to measure the strength of associations. The Wilson method was used to calculate 95% CIs for resistance proportions. A p-value <0.05 was considered statistically significant.

The study protocol was reviewed and approved by the Institutional Ethical Review Board of Nishtar Medical University and Hospital, Multan (Ref. No: NMU/IRB/1594, 08/22). Written informed consent was obtained from the parents or legal guardians of all participants prior to enrollment. Patient confidentiality was maintained by assigning unique identification codes, and no identifiable personal information was stored or reported. The study adhered to the ethical principles outlined in the Declaration of Helsinki.

Results

We enrolled 1,180 children with respiratory complaints over one year in Multan. Males 658 (55.8%) and females 522 (44.2%) (male: female 1.26:1) (Figure 1). Children <5 years accounted for 786 (66.6%), while ≥5 years were 394 (33.4%). Study cases belonged to different areas (Table 1).

Among study cases, upper respiratory tract infections (URTIs) were more frequent than lower respiratory tract infections (LRTIs): URTIs 842 (71.4%) vs LRTIs 338 (28.6%). Among URTIs, pharyngitis 408 (48.5%), tonsillitis 382 (45.4%), and otitis media 52 (6.2%); among LRTIs, pneumonia 291 (86.1% of LRTIs) and bronchiolitis 47 (13.9%) (Table 2).

Results showed that cases peaked during winter (November–January), contributing ~41.8% of all presentations, with a secondary rise during monsoon (July–August) (~22.3%). URTIs showed sharper winter seasonality, while LRTIs were more evenly spread (Table 3).

Cultures were performed for 615 (52.1%) children and were positive in 412 (67.0%). Culture positivity was higher

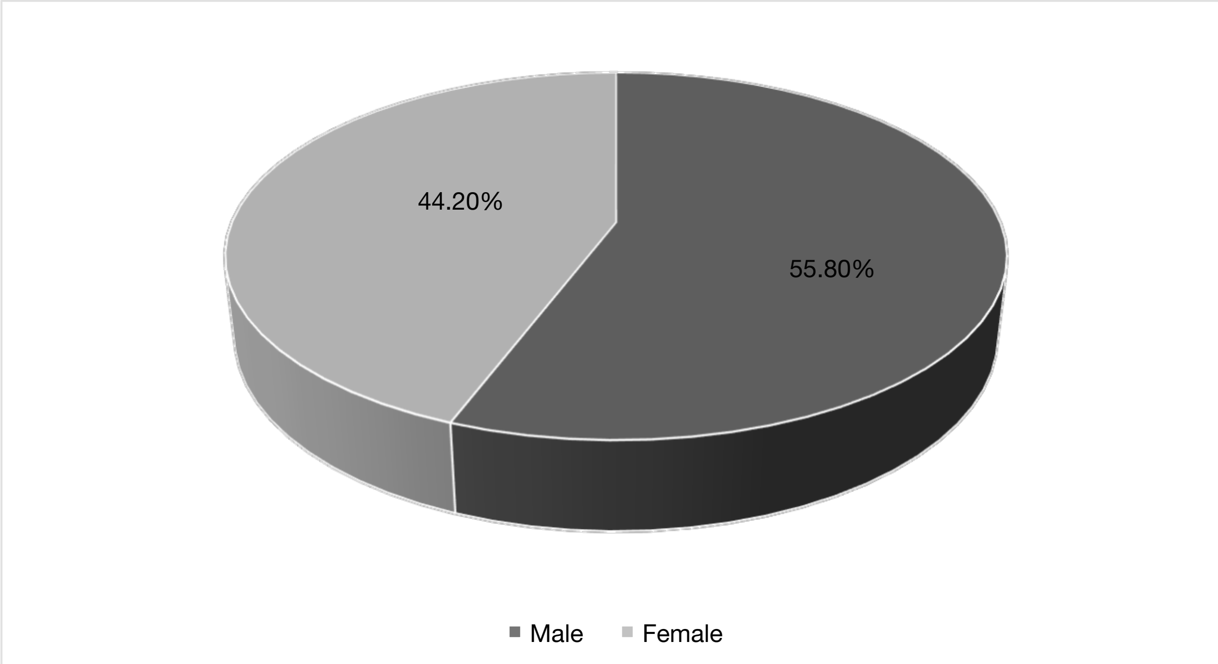

Figure 1. Gender based distribution of study cases

in LRTIs than URTIs (LRTI 300/380=78.9% vs URTI 112/235=47.7%; OR 4.12, 95% CI 2.89–5.88; χ^2=64.28, p<0.001) (Table 3).

Results showed that the leading pathogens isolated from the isolated samples from study cases were Streptococcus pneumoniae 38.8%, Haemophilus influenzae 26.5%, Moraxella catarrhalis 14.1%, Staphylococcus aureus 12.6%, and Klebsiella pneumoniae 8.0% among positive cultures (Figure 2).

The level of resistance to amoxicillin across the major respiratory pathogens was high, with S. pneumoniae demonstrating resistance in 52.4% (95% CI: 44.7-60.0) of isolates, H. influenzae in 61.2% (95% CI: 51.8-69.8), M. catarrhalis in 44.8%, (95% CI: 32.7-57.5), and K. pneumoniae in 68.1% (95% CI: 51.0-81.4). The level of resistance to azithromycin was moderate at approximately 28% - 36% within common bacterial isolates. Overall, antibiotic resistance for ceftriaxone and levofloxacin was better and was found mostly between 9% and 18% for most species. Finally, we note that methicillin resistant Staphylococcus aureus (MRSA) was found in 21.8% of all S. aureus isolates (95% CI: 12.7-34.7), which is a very important finding when considering empiric therapy options (Table 4).

Overall, 226 (19.1%) children required inpatient care. Hospitalization was far more frequent in LRTIs than URTIs (LRTI 192/338=56.8% vs URTI 34/842=4.0%; OR 31.25, 95% CI 20.84–46.86; χ^2=433.68, p<0.001) (Table 5). The mean length of stay was 5.2 ± 2.1 days. No deaths occurred.

When we compared the infection against gender, results showed that the proportion with LRTI did not differ significantly by sex (males 27.7% vs females 29.9%; χ^2=0.71, p=0.40). This study also showed that children <5 years had a higher odd of LRTI than those ≥5 years (<5: 252/786=32.1% vs ≥5: 86/394=21.8%; OR 1.69, 95% CI 1.27–2.24; χ^2=13.45, p<0.001).

Discussion

In this one-year, hospital-based cohort of 1,180 children from Multan, upper respiratory tract infections (URTIs) outnumbered lower respiratory tract infections (LRTIs), with the heaviest burden in younger age groups and clear winter–monsoon seasonality. Bacterial recovery from clinical specimens was modest, but when isolated, Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis, Klebsiella pneumoniae, and Staphylococcus aureus predominated. Antimicrobial susceptibility showed high resistance to amoxicillin among typical respiratory pathogens, intermediate resistance to azithromycin, and relatively preserved activity for ceftriaxone and levofloxacin; approximately one in five S. aureus isolates were MRSA. Taken together, these data provide a coherent local picture that aligns with national prescribing patterns and regional surveillance, while also underscoring opportunities for stewardship in first-line therapy.

Burden distribution and age pattern. The predominance of URTIs that we observed mirrors outpatient data from

Table 1. Demographic characteristics (n=1,180)

Variable	Frequency	Percentage
Age		
<5 years	786	66.6
≥5 years	394	33.4
Residency		
Rural	658	55.8
Urban	522	44.2

Pakistan showing that URTIs are frequent pediatric presentations and are often treated with antibiotics despite largely viral etiologies. Hospital point-prevalence surveys (PPS) likewise show respiratory infections as common indications for antibiotic use among children.[10]
The concentration of cases in younger ages, especially <5 years, is consistent with global and regional evidence of disproportionate LRTI risk and severity in early childhood and with Pakistan's influenza-associated disease burden estimates, which identify higher rates in pediatric populations. These convergent findings suggest our age and syndrome distribution is representative of pediatric respiratory epidemiology in Pakistan and similar LMIC settings.[10-14]
Our peaks during the cool months with a secondary monsoon rise parallel national sentinel estimates from Islamabad (2017–2019), which documented winter-dominant influenza circulation with measurable burden in children.[13] PERCH multi-country data likewise showed strong seasonal signatures in viral respiratory pathogens that drive pediatric pneumonia presentations.[14] The resonance between our single-center pattern and these external datasets strengthens confidence that the observed seasonality reflects true community transmission dynamics rather than site-level artifact.
The modest culture positivity we report is unsurprising in pediatric respiratory disease, where prior antibiotic exposure, low bacteremia rates in CAP, and challenges obtaining high-quality lower airway samples all reduce diagnostic yield. PERCH demonstrated that, across diverse African and Asian sites, viruses accounted for a substantial share of severe pediatric pneumonia, with classic bacteria comprising a smaller proportion than historically assumed.[14] In a study in 2023, Shahid et al., highlighted that broader analyses also report low detection rates of bacterial pathogens through blood cultures in children with community-acquired pneumonia (CAP).[15] Their findings reinforce the well-established

Table 2. Clinical spectrum of respiratory infections

Category	n (% of total)	% within category
URTI (n=842; 71.4%)		
Pharyngitis	408 (34.6)	48.5
Tonsillitis	382 (32.4)	45.4
Otitis media	52 (4.4)	6.2
LRTI (n=338; 28.6%)		
Pneumonia	291 (24.7)	86.1
Bronchiolitis	47 (4.0)	13.9

Table 3. Seasonal Distribution of Respiratory Infections

Season	Overall Cases (%)	URTIs Trend	LRTIs Trend
Winter (Nov–Jan)	41.8%	Sharp peak	Moderate presence
Monsoon (Jul–Aug)	22.3%	Slight increase	Moderate presence
Other Months	35.9%	Low activity	Even distribution

pattern of viral infections being the leading cause of CAP, especially among younger children. Results of the present study fit this pattern and argue for judicious testing strategies paired with strong infection-prevention measures and vaccination (e.g., influenza, pneumococcal), which can blunt seasonal surges and downstream antibiotic use.

Our findings on treatment practices align with broader prescribing trends seen across Pakistan. Previous prevalence surveys (PPS) consistently show that pediatric care relies heavily on empirical antibiotic use, with third-generation cephalosporins being prescribed particularly often. These reports also highlight how rarely treatment decisions are guided by microbiological testing, mirroring what we observed in our study population.[10] In primary care and outpatient settings, children with URTIs commonly receive antibiotics despite guideline-discordant indications.[5] At the macro level, national antibiotic consumption rose across 2019–2021 with substantial WATCH-class use, adding ecological pressure for resistance selection.[11] These converging strands, our clinical data, hospital PPS, outpatient surveys, and national consumption trends provide a coherent backdrop for interpreting the resistance we observed.[5,10,11]

Our finding of high amoxicillin resistance among *S. pneumoniae* 52.4% (95% CI: 44.7-60.0) of isolates, H. influenzae in 61.2% (95% CI: 51.8-69.8) with comparatively better activity for ceftriaxone and levofloxacin aligns with country-level respiratory surveillance. The JAC-AMR Pakistan country analysis synthesizing SOAR and related datasets documented substantial non-susceptibility among S. pneumoniae and H. influenzae to several oral agents, with β-lactam/β-lactamase inhibitor or parenteral third-generation cephalosporins retaining more consistent activity.[12] Earlier SOAR trend analyses

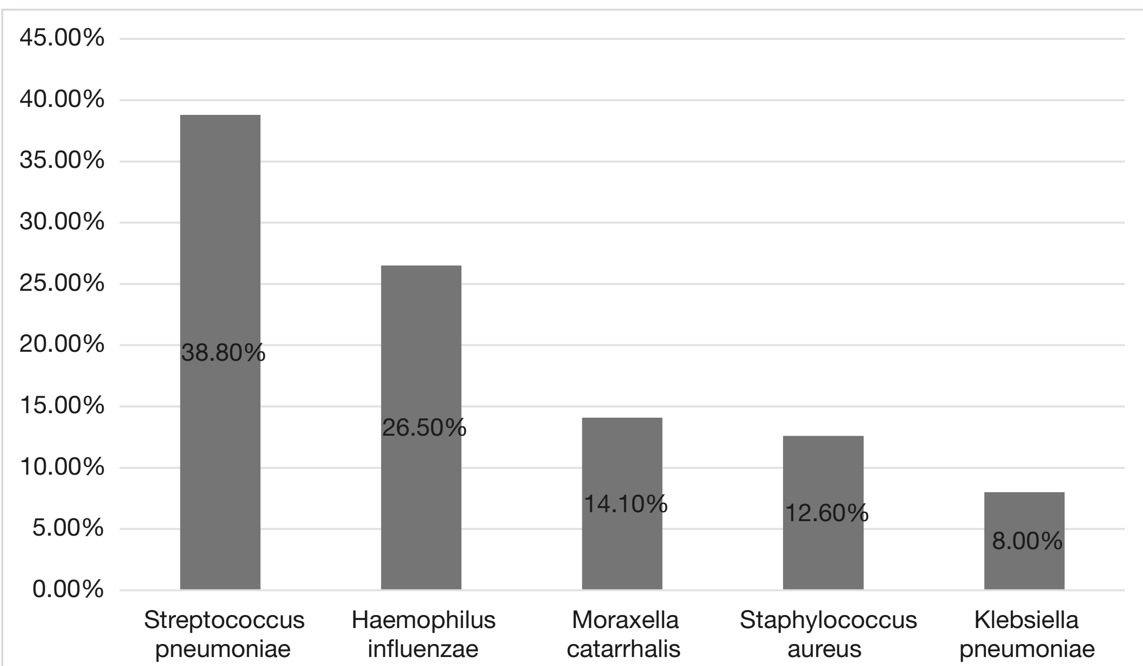

Figure 2. Frequency of different isolates in the present study

Table 4. Culture yield by clinical category (tested n=615)

Category	Tested n	Positive n (%)
URTI	235	112 (47.7)
LRTI	380	300 (78.9)
Total	615	412 (67.0)

also showed declining *S. pneumoniae* susceptibility to multiple agents across Pakistan, highlighting the clinical risk of amoxicillin (and macrolide) monotherapy in settings with elevated resistance.[16] Regionally, similar macrolide resistance and variable penicillin-class activity have been reported, reinforcing caution with azithromycin monotherapy for suspected bacterial URTI or CAP.[12,17] Within this context, our resistance profile is directionally consistent with both national synthesis and regional LMIC surveillance, adding contemporary Multan-specific estimates that can inform empiric choices.

Results of the present study showed that the level of resistance to azithromycin was moderate at approximately 28% - 36% within common bacterial isolates. This intermediate azithromycin resistance we observed (~one-third of typical organisms) echoes the Pakistan country report's caution that macrolide susceptibility among respiratory pathogens is unreliable in many sites. Hospital PPS reveal macrolides are frequently used empirically in Pakistan's children, often without microbiologic justification,[10] while outpatient URTI studies document substantial azithromycin prescribing for syndromes unlikely to benefit.[5] By contrast, ceftriaxone retained better activity in our isolates; PPS and consumption analyses confirm ceftriaxone's central role in empiric hospital therapy, although stewardship programs emphasize narrowing when possible to reduce WATCH-class pressure.[10,11,12]

Recovery of K. pneumoniae among LRTI cases with high amoxicillin and macrolide resistance is consistent with national patterns where Enterobacterales often exhibit resistance to multiple oral agents. For S. aureus, our MRSA fraction (~22%) sits within the range observed in Pakistani pediatric carriage studies after PCV10 introduction, which reported high S. aureus carriage with a considerable proportion MRSA among S. aureus isolates.[15] Although carriage is not equivalent to disease, these signals, together with hospital PPS showing frequent empiric anti-staphylococcal coverage,[10] support maintaining vigilance for MRSA in severe cases pending cultures. Importantly, our data do not justify routine MRSA coverage for all pediatric LRTIs; rather, they argue for targeted empiric therapy based on severity, local epidemiology, and risk factors, with rapid de-escalation when MRSA is unsubstantiated.[10,12,15]

Integrating our local resistance with national and regional evidence suggests several practice points. First, avoid macrolide monotherapy for presumed bacterial URTI or CAP given the resistance signal and low likelihood of benefit in viral disease. Second, for non-severe CAP in

Table 5. Antibiotic resistance (%) of common isolates with 95% CI

Organism (n)	Amoxicillin	Azithromycin	Ceftriaxone	Levofloxacin
S. pneumoniae (160)	52.4 (44.7–60.0)	28.1	12.5	9.4
H. influenzae (109)	61.2 (51.8–69.8)	32.1	15.6	12.8
M. catarrhalis (58)	44.8 (32.7–57.5)	35.0	10.3	8.6
S. aureus (52)	—	—	17.3	14.2
K. pneumoniae (33)	68.1 (51.0–81.4)	36.4	18.2	13.6
MRSA (% of S. aureus)	—	—	—	—
MRSA (52)	21.8 (12.7–34.7)			

Table 6. Hospitalization by clinical category

Category	Hospitalized n (%)	Not hospitalized n
URTI (n=842)	34 (4.0)	808
LRTI (n=338)	192 (56.8)	146
Total	226 (19.1)	954

immunized children, high-dose amoxicillin remains guideline-standard where penicillin-non-susceptibility is low; however, in Multan's current context, amoxicillin resistance >50% in key pathogens, amoxicillin/clavulanate or ceftriaxone (for hospitalized/severe cases) appears more defensible pending local stewardship review. Third, reserve fluoroquinolones for specific indications due to safety considerations despite favorable in-vitro activity, and promptly de-escalate as cultures and clinical trajectories allow. Finally, reinforcing vaccination and reducing inappropriate outpatient antibiotic use may meaningfully decrease seasonal peaks and selective pressure.

Strengths of the present study include prospective case accrual across a full epidemiologic year, standardized case definitions, and organism-specific resistance estimates with CIs. Limitations include single-center design, modest culture yield (inherent to pediatric respiratory disease), and potential confounding from prior antibiotics. Nonetheless, agreement of our estimates with Pakistani hospital PPS, outpatient surveys, and national consumption trends strengthens external validity, while concordance with country-level AMR syntheses supports the robustness of our susceptibility profile.

Conclusion

This one-year study provides a comprehensive overview of the clinical spectrum, microbiological profile, and antimicrobial resistance patterns of pediatric respiratory tract infections in Multan. URTIs predominated, but LRTIs were more common in children under five and carried a substantially higher risk of hospitalization. The high rates of amoxicillin resistance in key bacterial pathogens, coupled with moderate macrolide resistance, raise concerns over the continued empirical use of these agents without microbiological confirmation. Ceftriaxone and levofloxacin have retained better activity, but their use must be balanced with stewardship principles to prevent further resistance. The observed seasonal peaks underscore the importance of vaccination and heightened clinical vigilance during high-burden periods. These findings support the need for locally informed empiric therapy guidelines, strengthened antimicrobial stewardship programs, and expanded microbiological surveillance to improve pediatric respiratory care outcomes in Pakistan.

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