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Changes in the epidemiology and antimicrobial resistance patterns of *Streptococcus pneumoniae* from pediatric community acquired pneumonia patients attended in a Chinese hospital during the COVID-19 pandemic

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Abstract

Purpose The COVID-19 pandemic has altered the infection dynamics of numerous pathogens. This study aimed to elucidate its impact on *Streptococcus pneumoniae* (*S. pneumoniae*) infections in children with community acquired pneumonia (CAP).
Methods A retrospective analysis was conducted in pediatric CAP patients admitted before (2018–2019) and during (2020–2022) the COVID-19 pandemic. The epidemiology and antimicrobial resistance (AMR) patterns of *S. pneumoniae* were compared to reveal the impact of the pandemic.
Results A total of 968 *S. pneumoniae*-associated pediatric CAP patients were enrolled. Although the positivity rate and gender of patients were stable across both periods, the age notably increased in 2021 and 2022. Additionally, significant changes were observed in the co-infections with several pathogens and the resistance rates to certain antibiotics during the COVID-19 pandemic. The resistance rate to clindamycin and quinupristin-dalfopristin increased, whereas the resistance rate to tetracycline, trimethoprim-sulfamethoxazole, telithromycin, and proportion of multi-drug resistant isolates decreased. The number of *S. pneumoniae* strains and resistant isolates exhibited similar seasonal patterns in 2018 and 2019, peaking in November or December with another minor peak in March or April. During the COVID-19 pandemic, there was a sharp decrease in February 2020 and no resurgence was observed at the end of 2022. Additionally, the minor peak was absent in 2020 and shifted to other months in 2021 and 2022.
Conclusions The COVID-19 pandemic has markedly altered the infection spectrum of *S. pneumoniae* in pediatric CAP patients, as evidenced by shifts in the age of patients, respiratory co-infections, AMR patterns, and seasonal trends.

Keywords COVID-19 · *Streptococcus pneumoniae* · Epidemiology · Antimicrobial resistance · Community acquired pneumonia · Pediatrics

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Introduction

Community acquired pneumonia (CAP) remains a significant cause of morbidity and mortality globally, particularly affecting children under 5 years old and adults over 65 [1]. The advent of the pneumococcal conjugate vaccine (PCV) has markedly reduced the prevalence of *Streptococcus pneumoniae* (*S. pneumoniae*) and related hospitalizations [2]. In China, PCV7 became available in 2009 but was removed from the market in 2015. It was not until 2017 that PCV13 was introduced. The two-year gap in vaccine availability nullified the advantages gained from the previous PCV vaccination for pneumococcal disease [3]. Additionally, PCV vaccination has not been included in the national immunization program of China, leading to low vaccine coverage [4]. Notably, *S. pneumoniae* continues to be a prevalent pathogen in pediatric CAP and is a leading cause of lower respiratory infection deaths [5, 6]. In many healthcare settings, empirical antimicrobial therapy forms the bedrock of pediatric CAP management, often due to the unavailability of bacterial culture and antibiotic sensitivity test results [7]. Thus, the surveillance of antimicrobial resistance (AMR) patterns in common pathogens is crucial, as it aids in the informed empirical selection of antibiotics.

The infection spectrum and AMR trends of many pathogens have changed significantly since 2020 due to the COVID-19 pandemic. Notably, infections caused by *S. pneumoniae*, including both invasive pneumococcal diseases and non-invasive infections, have decreased in many countries during this period [8–12]. Additionally, the seasonal distribution of *S. pneumoniae* isolates and their AMR to certain antibiotics have evolved, as indicated by several studies [13–16]. However, most existing research has only covered a brief period within the pandemic and has not extensively focused on *S. pneumoniae* strains isolated from pediatric patients with CAP.

In light of this, the current study aims to assess the impact of the COVID-19 pandemic on the bacterial epidemiology and AMR patterns of *S. pneumoniae* strains isolated from pediatric CAP patients. Our study covers the period from 2018 to 2019 (pre-pandemic) and 2020–2022 (during the pandemic).

Materials and methods

Study population

The study was conducted retrospectively at Yongchuan Hospital of Chongqing Medical University from January 2018 to December 2022. Pediatric patients diagnosed with CAP were identified using a comprehensive approach that encompassed clinical features, chest imaging, and laboratory tests. The inclusion criteria covered patients aged from 1 month to 18 years. The exclusion criteria were: (1) Onset of pneumonia ≥ 48 h after hospital admission. (2) Chest radiography findings indicative of interstitial infiltrate, alveolar infiltrate, lobar pneumonia, or pleural effusion > 72 h after admission. (3) Lung infiltrate or interstitial changes interpreted as pulmonary tuberculosis, pulmonary edema, or atelectasis. (4) Patients with incomplete medical records or absent bacterial culture results. The ethics committee of Yongchuan Hospital approved the study protocol (No. 2023-KeLunShen-76).

S. pneumoniae strains isolation and antimicrobial susceptibility testing

Sputum samples were collected upon admission and submitted for microbiological testing according to established clinical protocols. For patients unable to expectorate sputum, samples were obtained either from the nasopharynx or by deep suction under negative pressure. Adequate sputum quality was defined as containing ≥ 25 leukocytes and ≤ 10 epithelial cells under low magnification. The specimens were cultivated on MacConkey, blood, and chocolate agar, and incubated at 37℃ in a 5% CO2 environment for 18–24 h. *S. pneumoniae* identification was performed using the Vitek-2 Compact system from BioMérieux, France and the minimum inhibitory concentrations (MICs) were determined using ATB identification cards. This study tested 14 antibiotics, including tetracycline, clindamycin, trimethoprim-sulfamethoxazole, erythromycin, telithromycin, chloramphenicol, quinupristin-dalfopristin, cefotaxime, amoxicillin, rifampicin, levofloxacin, moxifloxacin, linezolid, and vancomycin. *S. pneumoniae* isolates were classified as susceptible, intermediate, or resistant according to the MIC breakpoints of the Clinical and Laboratory Standards Institute (CLSI) criteria. This study included only unique *S. pneumoniae* isolates, excluding repeated isolates from the same patient during the same hospitalization episode. Multi-drug resistant (MDR) isolates were defined as resistance to three or more antibiotic classes [17]. Quality control was ensured using the *S. pneumoniae* ATCC49619 strain.

Identification of respiratory co-infections

Our research explored respiratory co-infections that involve bacteria, *Mycoplasma pneumoniae* (*M. pneumoniae*), and viruses in children suffering from *S. pneumoniae*-associated CAP. We specifically assessed bacterial co-infections for three isolates: *Moraxella catarrhalis* (*M. catarrhalis*), *Haemophilus influenzae* (*H. influenzae*), and *Staphylococcus*

aureus (*S. aureus*). Co-infections were identified through sputum specimens that tested positive for *S. pneumoniae* and at least one other bacterial species. To ascertain *M. pneumoniae* co-infections, venous blood samples were collected for serum isolation. Detection of *M. pneumoniae* was carried out by identifying Immunoglobulin M (IgM) antibodies in the serum using either an indirect immunofluorescence assay (IFA) or a passive particle agglutination test (Fujirebio, Japan), as per the manufacturer's guidelines. An antibody titer of ≥ 1:160 in the passive agglutination test was considered confirmatory of an *M. pneumoniae* infection.

Viral co-infections were determined by obtaining venous blood or nasopharyngeal swab samples from patients at admission. Our examination targeted five primary respiratory viruses: influenza virus A (IVA), influenza virus B (IVB), parainfluenza virus (PIV), respiratory syncytial virus (RSV), and adenovirus (ADV). Serum IgM antibodies for these viruses were measured using IFA from venous blood samples. Additionally, nasopharyngeal swab samples underwent analysis via a multiplex direct immunofluorescence assay kit (Diagnostic Hybrids, Athens, Ohio, USA), adhering to established procedures. The identification of viral co-infections was based on positive test results from either serum or nasopharyngeal swabs.

Statistical analysis

The assessment of the normality of quantitative data was performed using the Kolmogorov–Smirnov test. Data adhering to a normal distribution were presented as mean ± standard deviation (SD), and comparisons between groups were conducted using Student's t-test. Data not following a normal distribution were expressed as medians and interquartile ranges, with group comparisons performed using the Mann–Whitney U test. According to the actual frequency and theoretical frequency, categorical variables were compared via two-tailed chi-square test, Fisher's exact test, or Yates' continuity corrected chi-square test. Analyses of co-infections were conducted after the exclusion of patients who lacked corresponding pathogenic results. All statistics analyses were performed by using GraphPad Prism 9.0 Software (GraphPad Software, Inc., San Diego, CA, USA). $P < 0.05$ was considered to be statistically significant.

Results

Comparison of positivity rates, demographic characteristics, and respiratory co-infections in children with *S. pneumoniae*-associated CAP before and during the COVID-19 pandemic

Among 6115 children hospitalized for CAP, respiratory specimens were obtained from 5941 upon admission for bacterial culture. This process resulted in the identification of 968 non-duplicate *S. pneumoniae* isolates, all derived from sputum specimens. Despite a reduction in the number of isolates during the COVID-19 pandemic from 2020 to 2022, the positivity rate for *S. pneumoniae* remained stable. Patients with *S. pneumoniae*-associated CAP had a median age of 26 months, with 58.3% being males. The distribution of *S. pneumoniae* infections across various age groups was as follows: 27.4% (265 cases) in children under 1 year, 33.4% (323 cases) in children aged 1 to less than 3 years, 35.3% (342 cases) in children aged 3 to less than 6 years, 3.0% (29 cases) in children aged 6 to less than 10 years, and 0.9% (9 cases) in children aged 10 years and older. During the COVID-19 pandemic, the median age in 2021 and 2022 was significantly higher compared to that in 2018; however, no significant changes were observed in the gender distribution, as indicated in Table 1.

The most common symptoms of enrolled patients included cough (97.2% of patients), fever (41.1%), and wheezing (27.3%). In cases of bacterial co-infections, the incidence rates of *S. pneumoniae*-associated CAP patients co-infected with *M. catarrhalis*, *H. influenzae*, and *S. aureus* were 16.3%, 12.4%, and 1.4%, respectively. Notably, the co-infections with *M. catarrhalis* increased in both 2019 and 2020 compared to 2018. Similarly, *H. influenzae* co-infections exhibited significant fluctuations, with a lower rate in 2020 than 2019, but a higher rate in 2021 compared to 2018 ($P < 0.05$). Regarding other pathogens, 33.5% of the patients had co-infections with *M. pneumoniae*, and there were 155 cases of viral co-infections, predominantly with RSV. Despite a noticeable increase in *M. pneumoniae* co-infections in 2019, these rates significantly declined in the subsequent three years, with notably lower rates in 2021 and 2022 compared to 2019 ($P < 0.05$). In 2021, the co-infections with IVA were significantly reduced compared to 2019, and PIV co-infections decreased significantly compared to 2018 and 2019. Compared to pre-pandemic levels, RSV co-infections notably increased in 2020 but fell to the lowest level in 2022, all statistically significant ($P < 0.05$). However, the co-infections of *S. aureus*, IVB, and ADV did not exhibit significant changes during the COVID-19 pandemic, as detailed in Table 1.

Table 1 Comparison of positivity rates, demographic characteristics, and co-infection patterns in *S. pneumoniae*-associated CAP patients before and during the COVID-19 pandemic

Variables	Total	2018	2019	2020	2021	2022
S. pneumoniae-positives [No. (%)]	968 (16.3)	246 (16.3)	264 (16.2)	146 (16.7)	180 (17.4)	132 (14.7)
Age (months)	26 (10.25-43)	21 (10–39)	26 (11-42.75)	23.5 (9-41.25)	32 (11.25-47) [a]	37 (12–50) [a]
Male patients [No. (%)]	564 (58.3)	149 (60.6)	154 (58.3)	80 (54.8)	97 (53.9)	84 (63.6)
Respiratory co-infections [No. (%)]						
M. catarrhalis	158 (16.3)	29 (11.8)	49 (18.6) [a]	31 (21.2) [a]	30 (16.7)	19 (14.4)
H. influenzae	120 (12.4)	25 (10.2)	38 (14.4)	8 (5.5) [b]	32 (17.8) [a]	17 (12.9)
S. aureus	14 (1.4)	4 (1.6)	4 (1.5)	2 (1.4)	3 (1.7)	1 (0.8)
M. pneumoniae	287 (33.5)	62 (29.5)	99 (41.9) [a]	47 (35.6)	47 (28.3) [b]	32 (28.6) [b]
IVA	14 (1.5)	4 (1.7)	8 (3.0)	1 (0.7)	0 (0.0) [b]	1 (0.8)
IVB	7 (0.7)	2 (0.8)	1 (0.4)	4 (2.8)	0 (0.0)	0 (0.0)
PIV	34 (3.6)	9 (3.8)	12 (4.6)	10 (6.9)	0 (0.0) [a, b]	3 (2.8)
RSV	101 (10.6)	25 (10.5)	25 (9.5)	26 (18.1) [a, b]	22 (12.2)	3 (2.4) [a, b]
ADV	1 (0.1)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)

Continuous variable was presented as the median (25-75th percentiles); a: $P < 0.05$ Versus 2018; b: $P < 0.05$ Versus 2019

Table 2 Comparison of resistance rates of *S. pneumoniae* isolates before and during the COVID-19 pandemic

Antibiotics	No. (%) of resistant isolates					
	Total ($n = 968$)	2018 ($n = 246$)	2019 ($n = 264$)	2020 ($n = 146$)	2021 ($n = 180$)	2022 ($n = 132$)
Tetracycline	838 (86.6)	226 (91.9)	220 (83.3) [a]	132 (90.4)	154 (85.6) [a]	106 (80.3) [a]
Clindamycin	942 (97.3)	240 (97.6)	252 (95.5)	143 (97.9)	179 (99.4) [b]	128 (97.0)
Trimethoprim-sulfamethoxazole	747 (77.2)	207 (84.1)	201 (76.1) [a]	110 (75.3) [a]	138 (76.7)	91 (68.9) [a]
Erythromycin	959 (99.1)	244 (99.2)	262 (99.2)	145 (99.3)	179 (99.4)	129 (97.7)
Telithromycin	33 (3.4)	15 (6.1)	8 (3.0)	4 (2.7)	2 (1.1) [a]	4 (3.0)
Chloramphenicol	101 (10.4)	24 (9.8)	29 (11.0)	15 (10.3)	13 (7.2)	20 (15.2)
Quinupristin-dalfopristin	40 (4.1)	5 (2.0)	5 (1.9)	23 (15.8) [a, b]	6 (3.3)	1 (0.8)
Cefotaxime	10 (1.0)	8 (3.3)	1 (0.4) [a]	0 (0.0)	1 (0.6)	0 (0.0)
Amoxicillin	7 (0.7)	2 (0.8)	1 (0.4)	1 (0.7)	2 (1.1)	1 (0.8)
Rifampicin	3 (0.3)	2 (0.8)	0 (0.0)	0 (0.0)	1 (0. 6)	0 (0.0)
Levofloxacin	3 (0.3)	0 (0.0)	0 (0.0)	2 (1.4)	0 (0.0)	1 (0.8)
Moxifloxacin	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Linezolid	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Vancomycin	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
MDR isolates	886 (91.5)	233 (94.7)	240 (90.9)	137 (93.8)	162 (90.0)	114 (86.4) [a]

a: $P < 0.05$ Versus 2018; b: $P < 0.05$ Versus 2019

Comparison of drug resistance rates of *S. pneumoniae* isolates in pediatric CAP patients before and during the COVID-19 pandemic

As indicated in Table 2, the total resistance rates of *S. pneumoniae* to various antibiotics were as follows: tetracycline (86.6%), clindamycin (97.3%), trimethoprim-sulfamethoxazole (77.2%), erythromycin (99.1%), telithromycin (3.4%), chloramphenicol (10.4%), quinupristin-dalfopristin (4.1%), cefotaxime (1.0%), amoxicillin (0.7%), rifampicin (0.3%), and levofloxacin (0.3%). There were no isolates resistant to moxifloxacin, linezolid, and vancomycin. MDR isolates represented 91.5% (886 out of 968) of the cases. The predominant MDR pattern, exhibiting resistance to macrolides, lincosamides, tetracyclines, and sulfonamides, accounted for 66.4% of the MDR isolates. Notably, the resistance rates to tetracycline, trimethoprim-sulfamethoxazole, and cefotaxime significantly decreased in 2019 compared to 2018 ($P < 0.05$). During the COVID-19 pandemic, there were significant reductions in the resistance rates to tetracycline in 2021 and 2022, trimethoprim-sulfamethoxazole in 2020 and 2022, telithromycin in 2021, and the proportion of MDR isolates in 2022. Conversely, the resistance rate to clindamycin significantly increased in 2021 compared to 2019, and the resistance rate to quinupristin-dalfopristin in 2020 was significantly higher than the pre-pandemic levels ($P < 0.05$). The resistance rates to other antibiotics remained unchanged during the COVID-19 pandemic.

Changes in the seasonal patterns of *S. pneumoniae* strains and drug resistant isolates during the COVID-19 pandemic

As illustrated in Fig. 1, the number of *S. pneumoniae* isolates displayed seasonal trends in 2018 and 2019, with marked increases in October, peaking in November or December, and then declining to lower levels by February of the following year. The isolates experienced a minor surge in April, followed by a drop to the annual low in August or September. However, these seasonal distributions shifted during the COVID-19 pandemic. Notably, the isolates experienced a sharp decline in February 2020, and the typical resurgence observed between October and December was absent in 2022. Furthermore, the minor peak that usually occurred was missing in 2020 and shifted to May in 2021 and June in 2022. The seasonal trend of the positive rate of *S. pneumoniae* paralleled that of the isolates in most months of 2018 and 2019. However, from 2020 to 2022, the positive rate fluctuated and did not follow the usual seasonal patterns.

The *S. pneumoniae* isolates resistant to tetracycline, clindamycin, trimethoprim-sulfamethoxazole, and erythromycin also demonstrated seasonal distribution in 2018 and 2019. The pattern for these resistant isolates was similar to that of the total isolates. An exception occurred in 2018 when the minor peak for trimethoprim-sulfamethoxazole-resistant isolates shifted to March. During the COVID-19 pandemic, the seasonal patterns of resistant isolates underwent disruptions similar to those observed in total isolates, characterized by a sharp decrease in February 2020, an absence of resurgence at the end of 2022, and disappearance or shifts in minor peaks. Conversely, the seasonal patterns of drug resistance rates remained atypical throughout the five-year period, as depicted in Fig. 2A, B and C, and 2D.

Discussion

This study provides a comprehensive analysis of the impact of the COVID-19 pandemic on *S. pneumoniae* infections among pediatric CAP patients. The positivity rate and gender composition of the patients remained relatively consistent during the pandemic. However, there was a noticeable increase in patient age in 2021 and 2022 compared to 2018. Significant changes were also observed in the co-infections with certain pathogens. The *S. pneumoniae* isolates exhibited high resistance rates to tetracycline, clindamycin, trimethoprim-sulfamethoxazole, and erythromycin. During the COVID-19 pandemic, significant alterations were noted in the resistance rates to specific antibiotics and the proportion of MDR isolates. Moreover, the seasonal patterns of *S. pneumoniae* strains and resistant isolates shifted.

S. pneumoniae can colonize the nasopharynx of children asymptomatically, a crucial step in its transmission and subsequent infection. Apart from causing invasive diseases like bacteremia and meningitis, it more commonly affects the lower respiratory tract, leading to pneumonia [18]. In our study, 16.3% of pediatric CAP patients tested positive for *S. pneumoniae* in bacterial culture. This rate is lower than that observed in a Chinese cohort [19], but higher than those reported in two other studies [20, 21]. The COVID-19 pandemic has significantly altered the infection landscape of various pathogens in recent years. In our study, the number of *S. pneumoniae* isolates from pediatric CAP patients decreased notably between 2020 and 2022. Nonetheless, the positivity rate of *S. pneumoniae* isolates in bacterial cultures showed no significant changes during this period. Similar trends have been noted in other populations affected by invasive or non-invasive pneumococcal diseases during the pandemic [8–11, 22–24]. Non-pharmaceutical interventions (NPIs) implemented to control COVID-19, such as social distancing, mask-wearing, and school closures, are
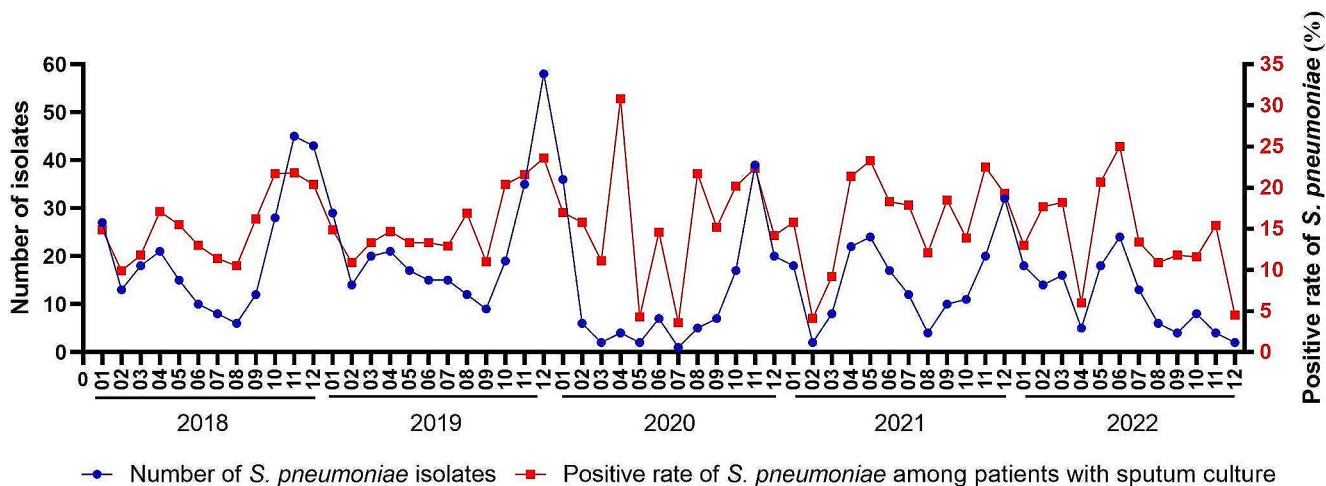

Fig. 1 Seasonal patterns in the number and positive rate of *S. pneumoniae* isolates from 2018 to 2022
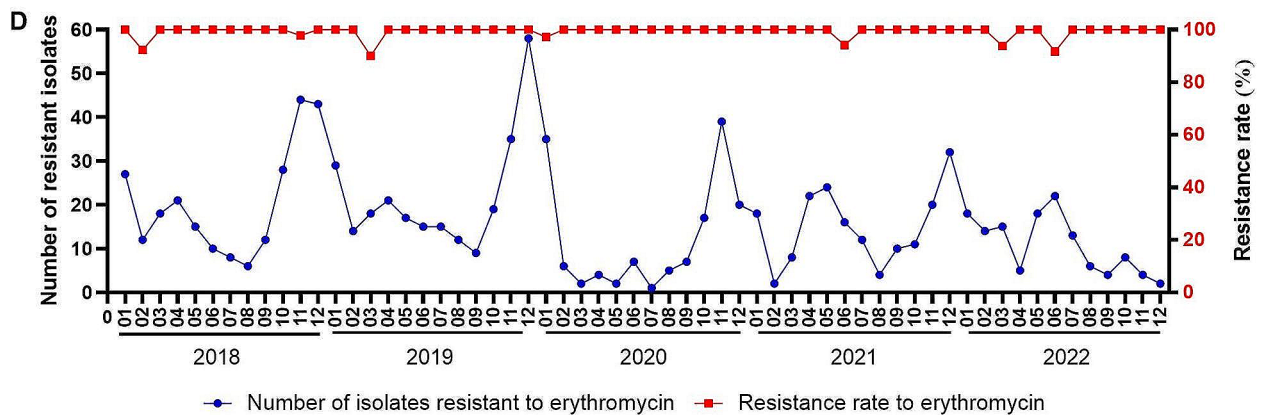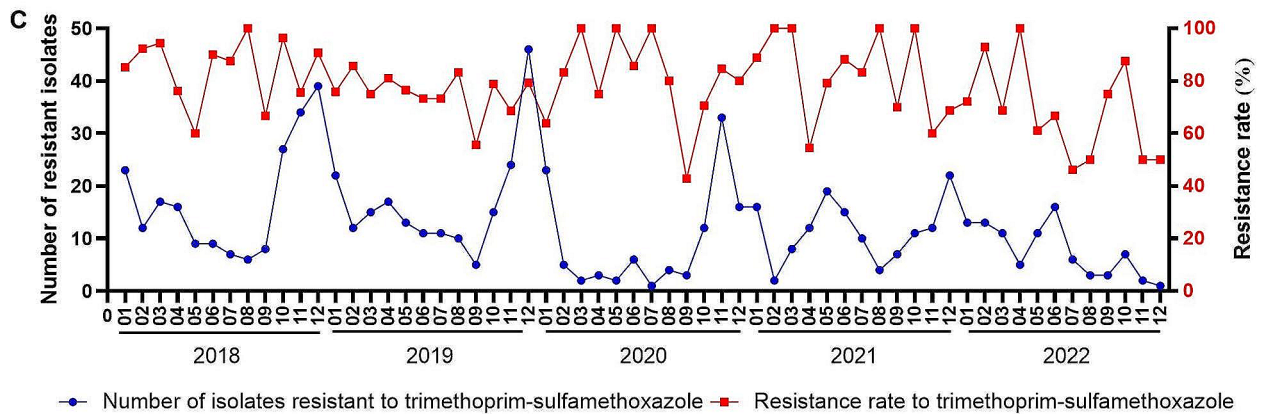
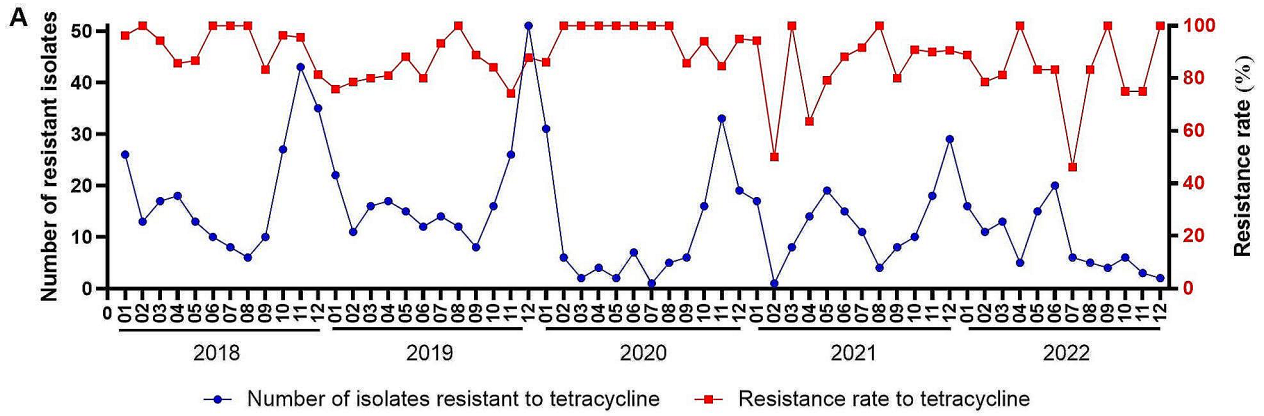Figure A: Number of isolates resistant to tetracycline / Resistance rate to tetracycline (2018–2022)

Figure B: Number of isolates resistant to clindamycin / Resistance rate to clindamycin (2018–2022)

Figure C: Number of isolates resistant to trimethoprim-sulfamethoxazole / Resistance rate to trimethoprim-sulfamethoxazole (2018–2022)

Figure D: Number of isolates resistant to erythromycin / Resistance rate to erythromycin (2018–2022)

Fig. 2 Seasonal patterns in the number and rate of *S. pneumoniae* isolates with drug resistance from 2018 to 2022. **(A)** Seasonal patterns in isolates with resistance to tetracycline. **(B)** Seasonal patterns in isolates with resistance to clindamycin. **(C)** Seasonal patterns in isolates with resistance to trimethoprim-sulfamethoxazole. **(D)** Seasonal patterns in isolates with resistance to erythromycin

thought to have reduced the transmission of *S. pneumoniae* and decreased the number of isolates [25–28]. Despite these measures, the rates of pneumococcal carriage and density among children and adults have remained relatively stable both before and during the pandemic [29–32]. In contrast, the incidence of pneumococcal CAP significantly decreased, mirroring the suppression of respiratory viruses such as RSV and influenza, which are critical in the pathogenesis of *S. pneumoniae* infections [29, 33, 34]. Notably, the rates of IVA and PIV co-infections in our study markedly declined in 2021. While there was a notable increase in 2020, RSV co-infections fell to their lowest level in 2022. Consequently, the reduction in *S. pneumoniae*-associated CAP cases is likely more influenced by the decreased incidence of co-infections with these viral agents than by the indirect effects of NPIs on carriage rates.

Except for a reduction in *S. pneumoniae* isolates, shifts have been observed in the age stages of infected patients during the COVID-19 pandemic [13]. In our study, the age of children with *S. pneumoniae*-associated CAP notably increased in 2021 and 2022 compared to 2018, a phenomenon that was absent in 2020. However, the gender composition did not significantly change throughout the pandemic. The adverse impact of respiratory co-infections on the severity and outcomes of pneumococcal pneumonia has been demonstrated [35]. Consistent with previous findings [19, 36], *S. pneumoniae-M. pneumoniae* and *S. pneumoniae*-RSV co-infection patterns were prevalent in pediatric CAP patients in our study. Additionally, *M. catarrhalis* and *H. influenzae* were common pathogens in bacterial co-infections, revealing distinct co-infection patterns of *S. pneumoniae* among children in the community setting. The pattern of co-infections in CAP patients has been affected by the COVID-19 pandemic [36]. In our study, aside from dramatic changes in viral co-infections, *M. pneumoniae* co-infections underwent significant decreases in 2021 and 2022. Contrary to the notable increase of *M. catarrhalis* co-infections in 2020, the *H. influenzae* co-infections exhibited a specific pattern, with a significant decrease in 2020 but an increase in 2021. These findings suggest that the effects of the COVID-19 pandemic might vary by pathogens.

AMR represents a significant threat to global health, contributing substantially to mortality worldwide. In 2019, bacterial AMR was associated with 4.95 million deaths, of which 1.27 million were directly attributable to bacterial AMR, with *S. pneumoniae* being a leading pathogen [37]. In

our study, the resistance rates of *S. pneumoniae* isolates to tetracycline, clindamycin, trimethoprim-sulfamethoxazole, and erythromycin were alarmingly high at 86.6%, 97.3%, 77.2%, and 99.1% respectively, indicating a significant resistance to tetracyclines, lincosamides, sulfonamides, and first-generation macrolides in strains isolated from pediatric CAP patients. Conversely, no resistance to moxifloxacin, linezolid, and vancomycin was observed throughout the study's five-year duration, aligning with previous findings in pediatric populations [38–41]. Furthermore, the high prevalence of MDR isolates in our study, which echoes findings from another study in China [42], can be attributed to factors like inappropriate antibiotic practices and patient self-medication. In our study, the resistance rates of *S. pneumoniae* to specific antibiotics exhibited significant alterations during the COVID-19 pandemic. Noteworthy reductions in resistance were observed for tetracycline, trimethoprim-sulfamethoxazole, telithromycin, and in the proportion of MDR isolates. In contrast, resistance to clindamycin and quinupristin-dalfopristin significantly increased in certain years. These pandemic-related shifts in AMR trends of *S. pneumoniae* have also been reported in various patient demographics [15, 16, 43–45]. Importantly, the introduction of PCV inoculation has markedly influenced the serotypes and AMR patterns of *S. pneumoniae* [46, 47]. Concurrently, there have been rises in the prevalence of potentially disease-causing AMR serotypes not covered by the vaccine [48]. Despite disruptions in PCV vaccination schedules, no significant changes in the serotype distribution of *S. pneumoniae* isolates were observed during the COVID-19 pandemic [16, 29]. Thus, the alterations in AMR patterns of *S. pneumoniae* during the pandemic may not be attributable to changes in serotypes.

Concerning seasonal patterns, *S. pneumoniae* infections are more common in cold season [49]. This pattern is possibly linked to colder temperatures, crowding, and increased respiratory viral infections in these months [18]. Similarly, *S. pneumoniae* isolates in our study peaked in November or December, but exhibited the lowest levels in August or September of 2018 and 2019. Additionally, a smaller peak was observed in April. However, the seasonal patterns underwent a shift in 2020 due to a pronounced decrease in February, and in 2022 due to the absence of a resurgence between October and December. These alterations coincided with local COVID-19 outbreaks in Chongqing. Furthermore, the April peak was not observed in 2020 and shifted to different months in 2021 and 2022. This shift was possibly due to stringent NPIs against COVID-19, which also prompted significant changes in the seasonality of *S. pneumoniae* isolates in other populations as well [13, 14, 30]. In our study, the positivity rate of *S. pneumoniae* exhibited a seasonal trend similar to that of isolates in most

months between 2018 and 2019, but fluctuated erratically without seasonal patterns from 2020 to 2022. The number of *S. pneumoniae* isolates resistant to tetracycline, clindamycin, trimethoprim-sulfamethoxazole, and erythromycin also displayed a seasonal distribution, nearly paralleling the patterns observed in total isolates during 2018 and 2019. Moreover, disruptions in the seasonal patterns of resistant isolates during the COVID-19 pandemic largely mirrored those of total isolates. However, the seasonal trends in the rate of resistant isolates remained atypical throughout the five-year period. These findings address the gaps in understanding *S. pneumoniae* infections among pediatric CAP patients during the COVID-19 pandemic and establish a baseline for future surveillance efforts.

This study, while insightful, is subject to several limitations. Firstly, PCV has not been included in China's national immunization program, and the serotypes of *S. pneumoniae* are not routinely detected in hospitals. As a retrospective study, the vaccine status of patients and the serotypes of the *S. pneumoniae* isolates remain unreported. This limitation hinders our ability to fully assess the influence of these factors on the AMR trends during the COVID-19 pandemic. Secondly, MICs are commonly employed parameters in the antimicrobial susceptibility studies [50]. While broth micro-dilution is the standard for determining MICs in antimicrobial susceptibility testing [17], our study utilized the Vitek-2 Compact system's automated dilution method [51]. This discrepancy might introduce measurement variations. Thirdly, the absence of detailed clinical data regarding disease severity, treatment approaches, and patient outcomes restricts our capacity for an in-depth analysis of disease dynamics. Fourthly, our study may be affected by survivorship bias. Some pediatric CAP patients might have recovered after receiving treatment in community hospitals. The *S. pneumoniae* strains in our study were isolated from a large tertiary hospital, which could potentially overstate the actual resistance rates found in broader community settings. Moreover, as a single center study, the findings regarding the bacterial epidemiology and AMR trends of *S. pneumoniae* may not be entirely representative of other regions.

Conclusions

In summary, this study analyzes the impact of the COVID-19 pandemic on *S. pneumoniae* infections in children with CAP. During the pandemic, despite the stable positivity rate and gender composition, there was a notable increase in the age of patients in 2021 and 2022. Significant changes were also observed in the co-infections with multiple respiratory pathogens, resistance rates of *S. pneumoniae* to certain antibiotics, and the proportion of MDR isolates. Moreover, the

typical seasonal patterns of *S. pneumoniae* strains and drug-resistant isolates shifted during the pandemic. These findings reveal that the infection spectrum of *S. pneumoniae* in pediatric CAP patients has dramatically changed during the COVID-19 pandemic. A multicenter study involving more participants is essential to continuously monitor *S. pneumoniae* infections in the post-COVID-19 era.

Declarations

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