Infection and Drug Resistance

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ORIGINAL RESEARCH

Investigating the Distribution and Antibiotic Resistance of Bacterial Pathogens in Clinical Specimens from a Chinese Maternal and Child Hospital: The Role of Environmental Factors

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Objective: To analyze bacterial distribution and antibiotic resistance in clinical specimens from a Chinese hospital for evaluating environmental factors' impact on pathogen prevalence.

Methods: From January 2017 to December 2021, we collected 42,854 clinical specimens from hospitalized children and women. The specimens were cultured on various agar plates and incubated at 35°C for 18–48 h. Their identification was performed using standard biochemical methods and Matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF), whereas antibiotic susceptibilities were determined using the VITEK 2 system. Concurrent environmental data from Wuhan were analyzed for correlations with pathogen prevalence using multiple linear stepwise regression.

Results: Of the 24,555 bacterial strains isolated, the majority were gram-positive, and sputum was the most common specimen type. *Haemophilus influenzae* and *Escherichia coli* were the most prevalent pathogens in sputum and urine samples, respectively. Notably, *H. influenzae* and *Streptococcus pneumoniae* affected children under 6 years of age the most. Furthermore, *H. influenzae* showed high ampicillin resistance but low cefotaxime resistance; *S. pneumoniae* was sensitive to penicillin G, and *E. coli* was resistant to ampicillin but sensitive to cefotetan. The prevalence of multidrug-resistant organisms was below national averages. In terms of seasonality, *H. influenzae* peaked during late winter and early spring, and environmental analysis indicated positive correlations between PM2.5 and PM10, and *H. influenzae* and *S. pneumoniae* prevalence. In addition, NO_2 levels were positively correlated with increased *S. aureus* and *M. catarrhalis* prevalence; *E coli* prevalence was negatively correlated with ozone levels.

Conclusion: This study provides valuable insights into the distribution and antibiotic resistance patterns of bacterial pathogens in maternal and child healthcare facilities in Wuhan, China. Environmental factors significantly influence the epidemiology of certain bacterial pathogens. Implementing integrated health strategies that combine microbial surveillance with environmental monitoring is needed to effectively manage and prevent bacterial infections.

Keywords: epidemiology, multidrug-resistant pathogens, seasonality, particulate matter

Introduction

Given that bacterial infections are responsible for numerous diseases with high morbidity and mortality rates, they are a significant threat to public health worldwide. These infections can be acquired from various sources, including contaminated water, food, and surfaces, and may also contract from infected individuals or animals.[1] To develop effective prevention and treatment strategies, it is crucial to understand the sources and distribution of the bacterial pathogens. Surveillance programs are used to identify the source and distribution of bacterial pathogens by monitoring the occurrence and spread of bacterial infections in specific locations or populations. These findings provide valuable

Received: 28 March 2024
Accepted: 28 May 2024
Published: 4 June 2024

information on the prevalence and incidence of bacterial infections as well as changes in bacterial strains and patterns of antibiotic resistance over time.[2]

Specific drug-resistant bacteria, such as methicillin-resistant *Staphylococcus aureus* (MRSA), carbapenem-resistant *Pseudomonas aeruginosa* (CR-PAE), carbapenem-resistant *Escherichia coli* (CR-ECO), carbapenem-resistant *Klebsiella pneumoniae* (CR-KPN), and carbapenem-resistant *Acinetobacter baumannii* (CR-ABA), pose a significant threat to public health.[3] These bacteria acquire resistance to multiple classes of antimicrobial agents, leaving fewer treatment options for the infected patients. MRSA is a leading cause of healthcare-associated infection.[4] CR-PAE, CR-ECO, CR-KPN, and CR-ABA are associated with healthcare-associated infections, particularly in immunocompromised patients, and have caused outbreaks in hospitals and long-term care facilities worldwide.[5]

The spread of infectious diseases in landscapes of changing climate cannot inherently be characterized with complete certainty because of the complexity and diversity of microbial populations. Nevertheless, it is well established that increases in environmental temperatures appreciably augment the multiplication of an array of pathogens.[6] Some studies have shown a correlation between viral etiology in hospitalized children, including meteorological factors (temperature and relative humidity), and air pollutants (PM 10, PM 2.5, and NO_2);[7,8] however, the correlation between these factors and pathogenic bacteria remains unknown. In addition, there is a notable gap in research investigating the correlations between average volume of precipitation, sunlight hours, and ozone (O_3) levels and the prevalence of various pathogens. Understanding the correlations between environmental changes and individual pathogens over time, both globally and regionally, is essential.[9] These insights are vital for anticipating and mitigating future bacteriological threats. By identifying how environmental factors influence pathogen behavior, we can devise public health strategies that are more effectively tailored to preempt outbreaks and manage disease prevalence. This understanding is particularly crucial for safeguarding vulnerable groups like children and pregnant women.

The purpose of this study was to retrospectively investigate and statistically analyze the bacterial culture samples of inpatients at the Wuhan Children's Hospital during 2017–2021 and dynamically analyze the distribution, epidemic trends, and drug sensitivity of isolated pathogens; the findings are expected to help prevent bacterial infections and guide the rational use of drugs in clinical practice. Moreover, the correlations between different pathogens and local environmental factors (climate and air pollution) were explored.

Materials and Methods

Study Design

This retrospective study was conducted to analyze the distribution and antibiotic resistance patterns of bacterial pathogens in clinical specimens and to explore the impact of environmental factors on the prevalence of these pathogens. The study spanned across 5 years (January 2017 to December 2021) and included a comprehensive dataset of clinical and environmental metrics. Clinical and environmental data related to climate and air quality were collected concurrently to investigate potential correlations between the incidence of pathogenic bacteria and environmental variables, including air pollutant levels and climatic changes. In addition, clinical and demographic data of patients, such as age, type of specimens, microbiology results, and antibiotic resistance patterns of the isolates, were obtained from the hospital's laboratory information system.

Sample Collection

Between January 2017 and December 2021, a total of 42,854 specimens were collected from hospitalized children and women. These specimens included blood, sputum, pus and secretions, urine, and other specimens clinically suspected of harboring an infection, and the specimens were sent to a microbiology laboratory for culture and identification. All sample collections strictly adhered to the "Basic Technical Standard for Clinical Microbiology Laboratory" (People's Republic of China Health Industry Standard WS/T 805—2022) to ensure the quality and consistency of the data. If multiple cultures from the same patient during hospitalization showed the same bacteria, only one result was recorded.

Bacterial Isolates and Antibiotic Susceptibility Tests

All sample inoculation and culturing were performed strictly in accordance with the "Basic Technical Standard for Clinical Microbiology Laboratory" (People's Republic of China Health Industry Standard WS/T 805—2022). In particular, various clinical specimens were inoculated onto blood agar, MacConkey agar, and chocolate agar (Guangzhou Detgerm Microbiological Science, China) and incubated at 35°C for 18–48 h to isolate the suspected bacterial colonies. Species identification of the isolates was conducted using standard biochemical methods supported by VITEK 2 compact system (BioMérieux SA, France) and Matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF; Bruker, Germany). The antibiotic susceptibilities of clinical isolates were determined using the VITEK 2 compact system following the instrument specifications, complemented by the Kirby-Bauer (KB) method, and the results were interpreted according to the Clinical and Laboratory Standards Institute (CLSI) criteria (M100, 31st Edition).[10] *E. coli* ATCC 25922, *S. aureus* ATCC 25923, and *P. aeruginosa* ATCC 27853 were used as the quality control strains.

Environmental Data

Wuhan is segmented into 13 administrative districts, which encompass a total of 176 environmental monitoring stations. Considering that most of the samples from hospitalized patients were sourced from these districts, we used the averaged data from all monitoring stations as the city-wide environmental indicators (outliers are excluded based on Grubbs' test). We obtained monthly environmental data, including climate and air pollution metrics, for the Wuhan region for 2017–2021 from two sources: the China National Meteorological Data Sharing System and the Department of Ecology and Environment of Hubei Province. Average temperature (°C), relative humidity (%), average volume of precipitation (mm), and sunlight hours (h) were chosen as climatic variables, and fine particulate matter (PM2.5), inhalable particulate matter (PM10), nitrogen dioxide (NO2), and ozone (O3) were chosen as air pollution variables. Monthly air pollutant concentrations were calculated as the mean per 24-h period, except for O_3, which was calculated as the flow-weighted mean concentration per 8-h period. The concentrations of air pollutants are presented in $\mu g/m^3$.

Statistical Analysis

SPSS 24.0 software was used for statistical analysis. Relationships between air pollutant concentrations and climatic variables with the main pathogens using multiple linear stepwise regression analysis. Statistical significance was set at P values < 0.05.

Results

Demographic Characteristics

Between 2017 and 2021, a total of 24,555 bacterial strains were isolated from inpatients, with 755 isolates from women and 23,800 from children in our study. The children were further categorized into age groups as follows: 10,124 infants (0–1 year old), 5469 toddlers (1–3 years old), 4477 preschool-aged children (3–6 years old), and 3730 school-aged children (6–18 years old). Across all age groups, including adults and children, there were 14,926 males and 9629 females.

Distribution of Bacterial Pathogens

In this study, we identified a predominance of gram-negative bacteria (54.70%) and gram-positive bacteria (44.57%), with fungi comprising a markedly smaller proportion (0.73%). The most frequently isolated bacteria were *Haemophilus influenzae, Streptococcus pneumoniae*, and *Staphylococcus aureus*, as detailed in Table 1. Sputum was the primary sample source (45.61%), followed by pus and secretions (31.90%) (Figure 1A). A notable decrease in isolates from sputum was observed in 2020, likely due to the COVID-19 pandemic's impact on sample collection, as detailed in Figure 1B. There were significant changes in the bacterial spectrum over the study period, particularly in 2020, coinciding with the global outbreak of COVID-19. Notably, *H. influenzae* and *S. pneumoniae* were the most prevalent pathogens in sputum samples, whereas *E. coli* was primarily found in urine samples. Figures 2A–D illustrate the annual fluctuations in the prevalence of key pathogens in different sample types.

Table 1 Distribution and Proportion of Pathogenic Bacteria from 2017 to 2021

Pathogens	Total N (%)	2017 N (%)	2018 N (%)	2019 N (%)	2020 N (%)	2021 N (%)
Gram-positive bacteria	*10,945(44.57)*	*2285(46.51)*	*2652(47.37)*	*2776(43.07)*	*1319(45.44)*	*1913(40.74)*
S. pneumoniae	*3900(15.88)*	*662(13.47)*	*1088(19.44)*	*1116(17.32)*	*381(13.10)*	*653(13.91)*
S. aureus	*3714(15.13)*	*791(17.92)*	*856(15.29)*	*941(14.60)*	*465(15.99)*	*661(14.08)*
E. faecium	*776(3.16)*	*185(3.77)*	*181(3.23)*	*178(2.76)*	*97(3.34)*	*135(2.87)*
E. faecalis	*649(2.64)*	*168(3.42)*	*120(2.14)*	*117(1.82)*	*105(3.61)*	*139(2.96)*
S. epidermidis	*480(1.95)*	*225(4.58)*	*186(3.32)*	*22(0.34)*	*18(0.62)*	*29(0.62)*
S. constellatus	*235(0.96)*	*8(0.16)*	*18(0.32)*	*78(1.21)*	*69(2.37)*	*62(1.32)*
S. agalactiae	*220(0.90)*	*25(0.51)*	*22(0.39)*	*110(1.71)*	*45(1.55)*	*18(0.38)*
S. anginosus	*170(0.69)*	*4(0.08)*	*7(0.13)*	*58(0.90)*	*41(1.41)*	*60(1.28)*
S. haemolyticus	*122(0.50)*	*75(1.53)*	*26(0.46)*	*10(0.16)*	*6(0.21)*	*5(0.11)*
S. pyogenes	*114(0.46)*	*23(0.47)*	*53(0.95)*	*25(0.39)*	*7(0.24)*	*6(0.13)*
other	*565(2.30)*	*119(24.22)*	*95(1.70)*	*121(1.88)*	*85(2.93)*	*145(3.09)*
Gram-negative bacteria	*13,431(54.70)*	*2577(52.45)*	*2907(51.93)*	*3634(56.38)*	*1564(53.88)*	*2749(58.54)*
H. influenzae	*4434(18.06)*	*744(15.14)*	*1142(20.40)*	*1462(22.68)*	*242(8.32)*	*844(17.97)*
E. coli	*3235(13.17)*	*770(15.67)*	*675(12.06)*	*705(10.94)*	*477(16.40)*	*608(12.95)*
M. catarrhalis	*1590(6.48)*	*61(1.24)*	*279(4.98)*	*593(9.20)*	*223(7.67)*	*434(9.24)*
K. pneumoniae	*1193(4.86)*	*386(7.86)*	*270(4.82)*	*212(3.29)*	*151(5.19)*	*174(3.71)*
Salmonella	*601(2.45)*	*78(1.59)*	*83(1.48)*	*144(2.23)*	*102(3.51)*	*195(4.15)*
P. aeruginosa	*545(2.22)*	*130(2.65)*	*113(2.02)*	*116(1.80)*	*79(2.72)*	*107(2.28)*
A. baumannii	*254(1.03)*	*73(1.49)*	*49(0.88)*	*68(1.06)*	*20(0.69)*	*44(0.94)*
E. cloacae	*218(0.89)*	*73(1.49)*	*45(0.80)*	*38(0.59)*	*31(1.07)*	*31(0.66)*
S. maltophilia	*163(0.66)*	*38(0.77)*	*33(0.59)*	*40(0.62)*	*23(0.79)*	*29(0.62)*
K. aerogenes	*120(0.49)*	*50(1.02)*	*20(0.36)*	*24(0.37)*	*13(0.45)*	*13(0.28)*
other	*1078(4.39)*	*174(3.54)*	*198(3.54)*	*232(3.60)*	*203(6.99)*	*270(5.75)*
fungi	*179(0.73)*	*51(1.04)*	*39(0.70)*	*35(0.54)*	*20(0.69)*	*34(0.72)*
C. albicans	*117(0.48)*	*39(0.79)*	*33(0.59)*	*19(0.29)*	*11(0.38)*	*15(0.32)*
C. tropicalis	*16(0.07)*	*2(0.04)*	*1(0.12)*	*3(0.05)*	*4(0.14)*	*6(0.13)*
C. parapsilosis	*12(0.05)*	*1(0.02)*	*1(0.12)*	*7(0.11)*	*1(0.03)*	*2(0.04)*
C. glabrata	*9(0.04)*	*4(0.08)*	*1(0.12)*	*0(0)*	*2(0.07)*	*2(0.04)*
other	*25(0.10)*	*4(0.08)*	*3(0.05)*	*6(0.09)*	*2(0.07)*	*9(0.19)*
Total	*24,555*	*4913*	*5598*	*6445*	*2903*	*4696*

Age Distribution Prevalence Characteristics of Main Pathogens

Our analysis identified distinct patterns in the prevalence of pathogens across age groups. Notably, *H. influenzae* and *S. pneumoniae* were the predominant pathogens in children aged under 6 years. In addition, *E. coli* was most prevalent among school-aged children (30.72%), whereas *S. aureus* was the most common in adults (39.47%). Furthermore, the prevalence of both *H. influenzae* and *S. pneumoniae* gradually decreased with the age increasing beyond three years, as shown in Table 2.

Drug Resistance of Main Pathogens to Common Antimicrobials

Throughout the study period from 2017 to 2021, evolving resistance patterns were documented among key pathogens. *H. influenzae* saw an increase in resistance to ampicillin, escalating from 51.8% to 81.9%, and it showed similar trends for trimethoprim–sulfamethoxazole and azithromycin, with resistance peaking at 83.6% and 59.4%, respectively. Conversely, resistance to cefotaxime remained exceptionally low, consistently below 1% from 2019 to 2021(Supplementary Table 1). Resistance rates to penicillin G and amoxicillin in *S. pneumoniae* have gradually decreased from 2017 to 2021, as shown in Supplementary Table 2. Interestingly, *S. aureus* consistently showed resistance to penicillin, exceeding 95% (Supplementary Table 3), and *E. coli* showed high resistance to ampicillin, approaching 90%; however, it was markedly susceptible to

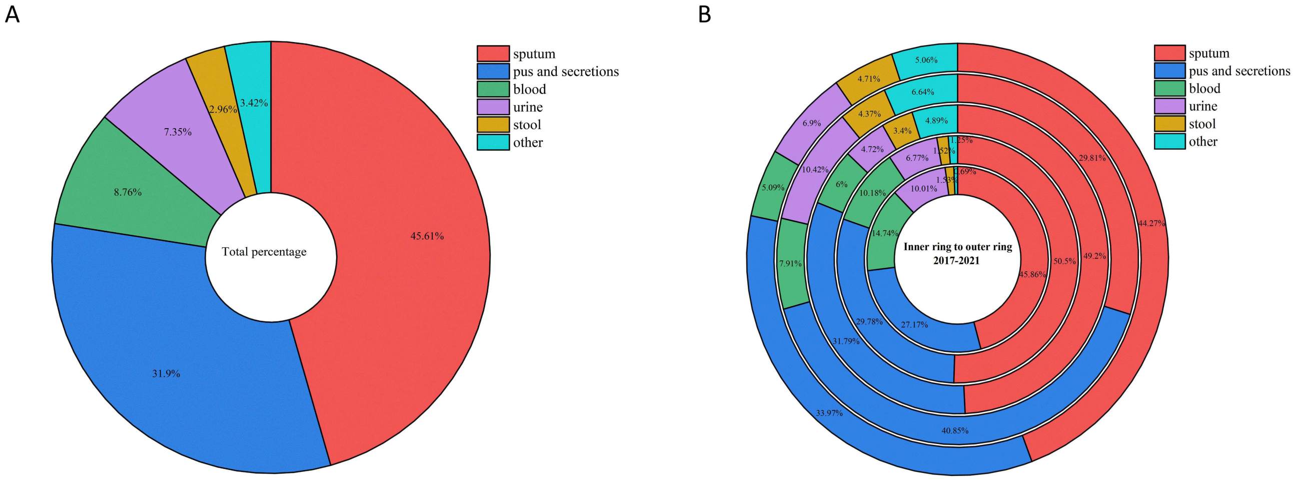

Figure 1 (**A**) Percentage of positive culture from various specimen types during study period. (**B**) Percentage of positive culture from various specimen types per year from 2017–2021.

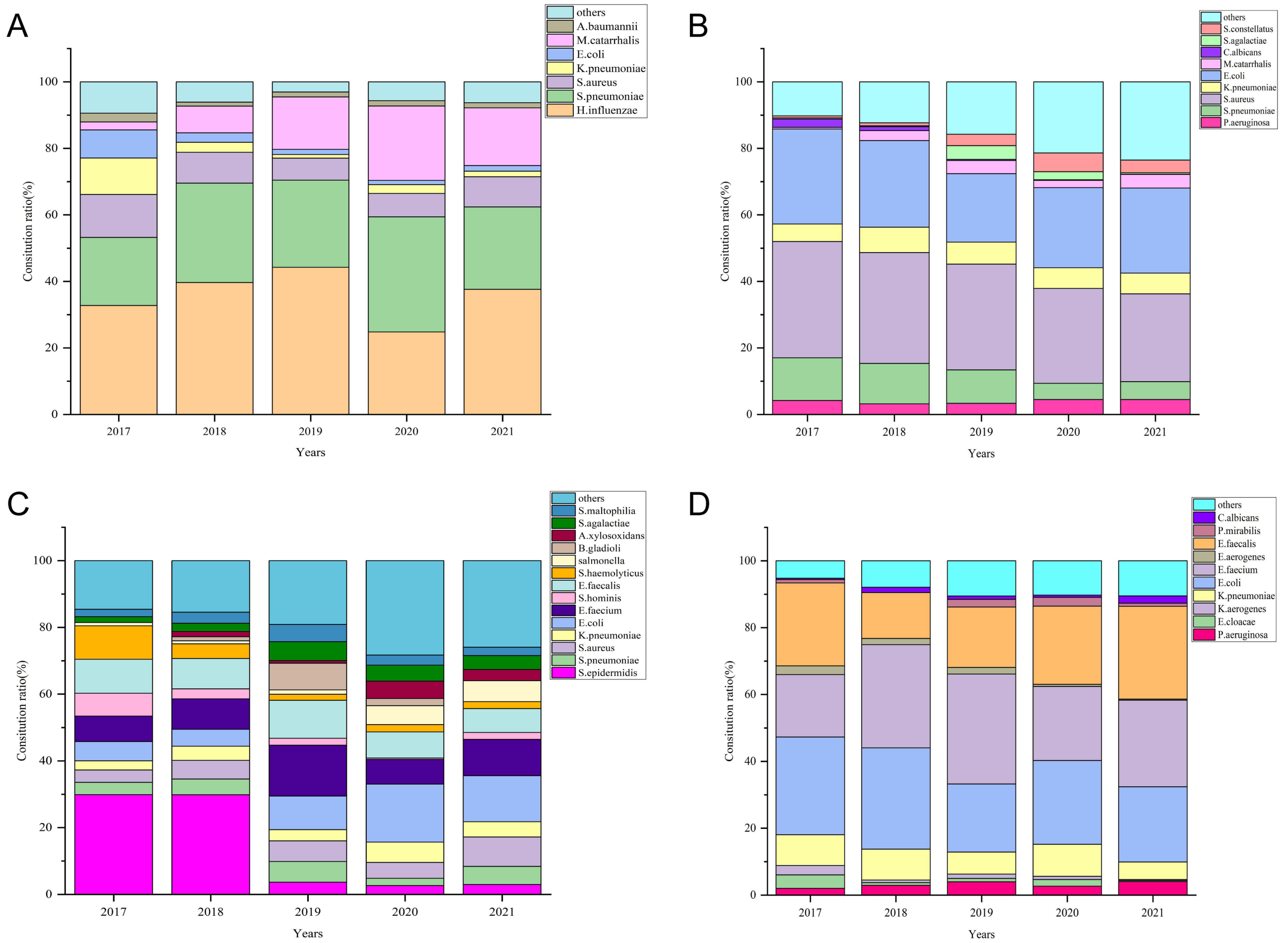

Figure 2 (**A**) Distribution of main bacteria in sputum from 2017–2021. (**B**) Distribution of main bacteria in pus and secretions from 2017–2021. (**C**) Distribution of main bacteria in blood from 2017–2021. (**D**) Distribution of main bacteria in urine from 2017–2021.

Table 2 Composition Ratio of Pathogens at Different Ages

	Infant (0–1 years old)	**Toddler (1–3 years old)**	**Preschool age (3–6 years old)**	**School age (6–18 years old)**	**Adult (>18 years old)**
H. influenzae	1889(18.66)	1320(24.14)	944(21.09)	271(7.27)	5(0.66)
S. aureus	1829(18.07)	634(11.59)	464(10.36)	474(12.67)	298(39.47)
S. pneumoniae	1610(15.90)	1130(20.66)	893(19.95)	259(6.94)	6(0.79)
E. coli	993(9.81)	417(7.62)	582(13.00)	1146(30.72)	87(11,52)
K. pneumoniae	677(6.69)	153(2.80)	116(2.59)	216(5.79)	23(3.05)
M. catarrhalis	619(6.11)	480(8.78)	432(9.65)	58(1.55)	0(0)
E. faecium	516(5.10)	124(2.27)	47(1.05)	66(1.77)	18(2.38)
E. faecalis	423(4.18)	76(1.39)	53(1.18)	67(1.79)	22(2.91)
salmonella	194(1.92)	254(4.64)	111(2.48)	42(1.13)	0(0)
S. epidermidis	190(1.88)	124(2.27)	55(1.23)	78(2.09)	31(4.11)
A. baumannii	114(1.13)	65(1.19)	29(0.65)	43(1.15)	3(0.40)
P. aeruginosa	110(1.09)	81(1.48)	155(3.46)	197(5.28)	2(0.26)
E. cloacae	94(0.93)	47(0.86)	26(0.58)	45(1.21)	5(0.66)
S. agalactiae	69(0.68)	11(0.20)	6(0.13)	4(0.11)	128(16.95)
S. maltophilia	67(0.66)	47(0.86)	20(0.45)	28(0.75)	1(0.13)
E. aerogenes	62(0.61)	26(0.46)	17(0.38)	9(0.24)	6(0.79)
S. constellatus	9(0.09)	26(0.46)	82(1.83)	118(3.16)	0(0)
S. angina	10(0.10)	31(0.57)	47(1.05)	78(2.09)	4(0.53)
other	649(6.41)	423(7.73)	398(8.89)	531(14.24)	116(15.36)
total	10,124	5469	4477	3730	755

cefotetan, piperacillin-tazobactam, and amikacin, as detailed in Supplementary Table 4. In addition, *K. pneumoniae*'s resistance to gentamicin significantly decreased from 39.7% to 9.1% from 2017 to 2021. By 2021, the resistance of *K. pneumoniae* to imipenem and meropenem was ~10%, as shown in Supplementary Table 5. *Moraxella catarrhalis* also showed a significant reduction in azithromycin resistance, which declined from 52.5% to 22.8% from 2017 to 2021, and furthermore, it showed low resistance to cephalosporins (Supplementary Table 6).

Distribution of Multidrug-Resistant Organisms (MDROs)

Throughout the study period, significant trends in the prevalence of MDROs were documented. The prevalence of MRSA decreased from 34.3% in 2018 to 29.8% in 2021. The detection rates of CR-PAE also dramatically dropped from 17.3% to 3.74% over the same period. In contrast, the detection rate for CR-ABA increased consistently, peaking at 45.45% in 2021. The detection rates for CR-ECO remained stable, whereas those for CR-KPN showed significant fluctuations. Notably, no cases of vancomycin-resistant *Enterococcus faecalis* (VREM) or penicillin-resistant *S. pneumoniae* (PRSP) were detected. Our findings, compared with the National Bacterial Resistance Network, show lower rates for CR-ABA and CR-PAE but higher rates for CR-ECO and CR-KPN, as detailed in Figure 3.

Seasonal Distribution of Main Pathogens

Overall, during the 5-year study period, *H. influenzae* showed similar seasonal patterns and clear prevalence peaks every year (except for 2020). Every year, the *H. influenzae* detection rate peaked during the change of season from winter to spring (February–April), and *M. catarrhalis* and *S. pneumoniae* detection rates peaked when summer turned to autumn. *H. influenzae, M. catarrhalis*, and *S. aureus* declined significantly by 2020 (Figure 4).

Multiple Regression Analysis of the Association Between Number of Isolates with Main Pathogens and Environmental Factors

Considering the correlation between various environmental factors (co-linearity), a multiple linear stepwise regression analysis was conducted with the number of samples detected for the six main pathogens (*H. influenzae, S. pneumoniae,*

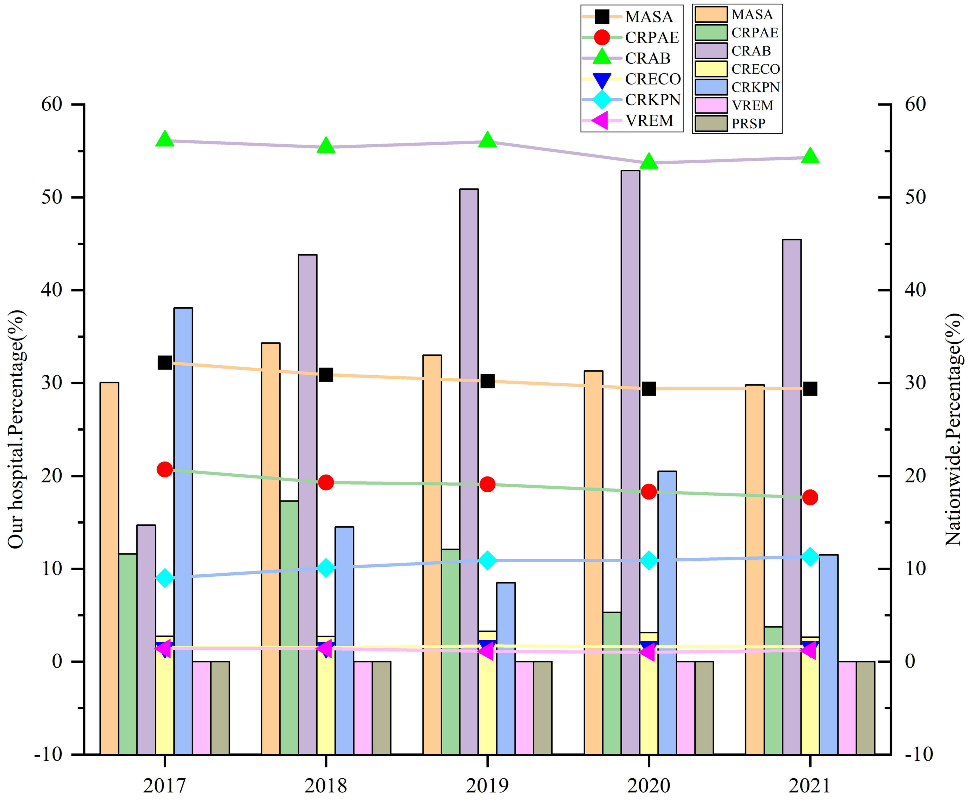

Figure 3 The trend in detection rates of multidrug-resistant organisms (MDROs) from 2017 to 2021 in our hospital and nationwide. The bar graph on the Y-axis represents the detection rates of multidrug-resistant organisms in our hospital; the line graph represents the national detection rates of MDROs. The X-axis represents the years.

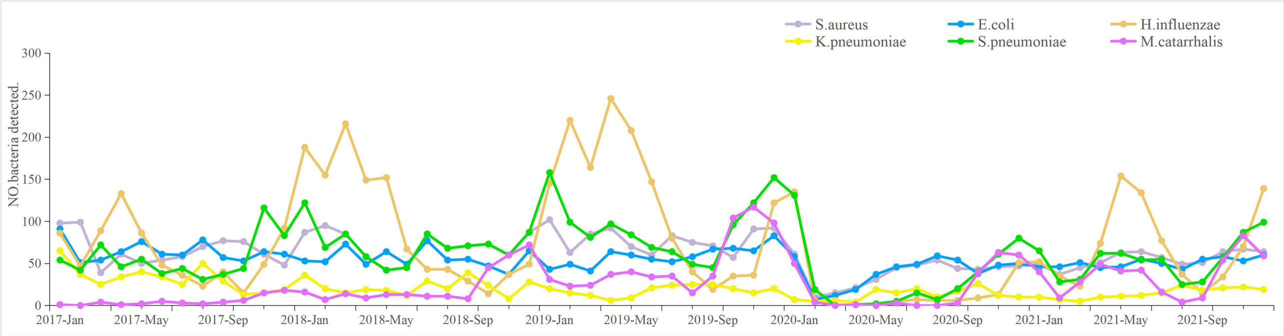

Figure 4 Seasonal distribution of H. influenzae, (S) pneumoniae, (S) aureus, (E) coli, (M) catarrhalis, and K. pneumoniae.

S. aureus, E. coli, M. catarrhalis, and *K. pneumoniae*) as the dependent variable, and monthly sunshine hours, average temperature, relative humidity, volume of precipitation, and PM2.5, PM10, NO_2, and O_3 concentrations as the independent variables (Table 3). The analysis resulted in six models with adjusted R^2 values ranging from 0.112 to 0.338, suggesting variable explanatory power across different pathogens. The number of *H. influenzae*-positive samples was positively correlated with PM10 concentration (coefficient = 0.386, $P < 0.05$). The number of *S. pneumoniae*-positive samples was positively correlated with PM2.5 (coefficient = 0.591, $P < 0.001$). The number of *S. aureus*- and *M. catarrhalis*-positive samples were positively correlated with NO_2 concentration (coefficient = 0.357 and 0.398, respectively; $P < 0.05$). The number of *E. coli*-positive samples were positively correlated with PM10 and average temperature (coefficient = 0.784 and 1.139, respectively; $P < 0.05$) and negatively correlated with relative O_3 (coefficient = −0.562, $P < 0.05$). The number of *K. pneumoniae*-positive samples were positively correlated with PM2.5 and average

Table 3 Mutiple Linear Stepwise Regression Analysis Model for Correlation Between Air Pollution Concentration, Meteorological Factor and Main Pathogens

Pathogen	Model summary		Correlation coefficients		
	Model significance (ANOVA)	**Adjusted R2**	**Air pollution concentration and Meteorological factor**	**Standard coefficient**	**P value**
H. influenzae	p <0.05	0.135	PM10 (μg/m3)	0.386	0.002
S. pneumoniae	p <0.001	0.338	PM2.5 (μg/m3)	0.591	0.000
S. aureus	p <0.05	0.112	NO2 (μg/m3)	0.357	0.005
E. coli	p <0.001	0.328	PM10 (μg/m3)	0.784	0.000
			O3 (μg/m3)	−0.562	0.021
			Average temperature (°C)	1.139	0.000
M. catarrhalis	p <0.05	0.144	NO2 (μg/m3)	0.398	0.002
K. pneumoniae	p <0.001	0.298	PM2.5 (μg/m3)	1.071	0.000
			Average temperature (°C)	1.028	0.000

temperature (coefficient = 1.071 and 1.028, respectively; $P < 0.05$) (Supplementary Figures 1–5). Variables such as relative humidity, average volume of precipitation, and sunlight hours were excluded from the final models because of their statistically insignificant influence.

Discussion

Our findings revealed that *S. pneumoniae* was the most common gram-positive bacterium and *H. influenzae* was the most common gram-negative bacterium; these findings are not consistent with previous reports.[11,12] Among all specimen types, sputum samples had the highest pathogen positivity rate; however, Chanda et al reported in their study that the most common pathogen-positive specimens in hospitalized patients were urine samples, blood samples, and wound swabs, and the most common microorganisms were coliforms.[13] Furthermore, blood culture analyses revealed a shifting prevalence of predominant bacteria. The observed decline in *S. epidermidis* detection coincides with improved infection control practices, notably the improved hand hygiene practices following the implementation of evidence-based policies, which significantly reduced false-positive rates in coagulase-negative staphylococcal cultures.[14] These results indicate that the distribution of bacteria and specimen sources differed among different regions and populations.

The variability in bacterial prevalence among different age groups was pronounced, particularly for *H. influenzae* and *S. pneumoniae*, which were the most prevalent in children aged under 6 years. This variability may be due to several factors. First, neither the *H. influenzae* type b (Hib) vaccine nor the thirteen-valent pneumococcal conjugate vaccine (PCV13) is included in China's national immunization program, leading to low voluntary vaccination rates. In addition, inconsistencies in vaccine timeliness and completion have also contributed to this issue.[15,16] Furthermore, the 76-day COVID-19 blockade significantly disrupted vaccinations, including those for Hib and PCV13, impacting overall vaccination rates. These factors together explain the significant prevalence of these pathogens among younger children.

In China, the rate of ampicillin resistance in *H. influenzae* strains increased steadily from 12% in 2000–2002 to 58.1% in 2016.[17] The current study revealed an even higher ampicillin resistance rate (88.4%). This significant increase indicated a rapid increase in ampicillin resistance among *H. influenzae* isolates in China. However, the resistance rate to cefotaxime was <1%, which was much lower than that reported in Iran (33.1%).[18] Therefore, third-generation cephalosporins such as cefotaxime could be considered the preferred treatment option for infections caused by ampicillin-resistant *H. influenzae* in China. Importantly, the majority of strains included in our study were isolated from respiratory tract samples. In China, azithromycin is commonly used as an empirical medication for respiratory tract infections in children. A multicenter study showed that the resistance rate of *H. influenzae* to azithromycin increased as follows: 29.89% in 2017, 37.55% in 2018, and 42.04% in 2019.[19] Therefore, the widespread use of azithromycin, coupled with increasing antibiotic resistance rates, may have contributed to the observed high level of azithromycin resistance.

S.pneumoniae is a prominent pathogen responsible for acute respiratory infections worldwide, and its antibiotic resistance rate varies significantly among children from different geographical areas.[20] Based on our findings, penicillin G could be considered as the first-line treatment for pneumococcal infections in children, particularly in Wuhan. We found *E. coli* exhibited a low resistance to cefotetan. Cefotetan, a cephamycin antibiotic developed in the 1980s, is a broad-spectrum antibiotic against gram-negative bacteria with potential as a carbapenem-sparing treatment option.[21] Notably, *K. pneumoniae* exhibited higher susceptibility to carbapenems and aminoglycosides such as amikacin and gentamicin, thus corroborating a previous report by Xu et al.[22] Our study further supports the notion that aminoglycosides and carbapenems are preferred therapeutic agents for treating *K. pneumoniae* infections in Wuhan.

Few studies have evaluated the prevalence of MDRO in pediatric patients. The prevalence of MDROs like MRSA has shown a slow decline, which is consistent with the trends reported by the China Antimicrobial Surveillance Network (CHINET), suggesting the effectiveness of enhanced infection control and antibiotic stewardship programs.[23] Despite the relatively lower detection rates of CR-ABA and CR-PAE compared to the national average levels, their presence remains concerning due to their association with high mortality and resistance.[24] In addition, although the absence of VREM and PRSP from 2017 to 2021 is encouraging, it is important to note that these pathogens continue to pose a significant threat to global health. Vancomycin-resistant enterococci (VRE), in particular, are considered a priority pathogen by the World Health Organization due to their high level of antimicrobial resistance and ability to cause severe infections.[25]

The seasonal distribution of key pathogens, particularly *H. influenzae*, plays a crucial role in shaping prevention and control strategies for bacterial infections. Our findings show that the prevalence of *H. influenzae* infection typically peaks from February to April every year, a pattern that was also noted by regional studies in Zhejiang, China.[26] However, deviations from this pattern have also been noted, such as in Chengdu, where peak detections were noted in May and November,[27] and this difference may be attributable to climatic differences across regions. The substantial decline in detection rates of several pathogens, such as *H. influenzae, M. catarrhalis*, and *S. aureus*, in 2020 is notably linked to the COVID-19 pandemic's profound impact on public health practices and social behaviors, including reduced travel and human interactions. These changes have significantly influenced pathogen transmission dynamics. Understanding these seasonal and situational factors is vital for developing effective infection control strategies that are tailored to specific environmental and societal contexts. Future studies should continue to investigate the underlying mechanisms linking seasonal changes to bacterial infection rates and refine strategies to more effectively prevent and manage these infections throughout the year.

To our knowledge, this is the first large-scale epidemiological investigation to comprehensively examine the relationship between meteorological factors and pathogenic infections in hospitalized children and women. This retrospective cohort study spanned five years and aimed to elucidate the potential associations between various meteorological parameters and the detection rates of *H. influenzae, S. pneumoniae, S. aureus, M. catarrhalis*, and *E. coli*. Our findings reveal interesting associations between meteorological factors and specific pathogens. We found that higher levels of particulate matter PM10 and PM2.5 in the air were associated with increased detection rates of *H. influenzae, S. pneumoniae*, and *K. pneumoniae*. A study in Suzhou, China also reported PM10 as an independent risk factor for the detection of *H. influenzae*.[28] This suggests that particles in air act as carriers that facilitate the transmission of these pathogens into the respiratory system. Furthermore, we observed a correlation between NO_2 concentrations and increased detection of *S. aureus* and *M. catarrhalis*. NO_2 may adversely affect the immune system, potentially weakening the body's defense against these pathogens. Interestingly, higher average temperatures were associated with higher detection rates for *E. coli* and *K. pneumoniae*. This could be attributed to the increased temperature, which creates a more favorable environment for the growth and reproduction of these pathogens. Conversely, a negative correlation was observed between the relative concentration of O_3 and detection rate of *E. coli*. This may be attributed to the antimicrobial properties of ozone because higher O_3 levels can inhibit the growth of *E. coli*. Although the adjusted R^2 values in our models are relatively low, they importantly highlight the complex and multifactorial nature of pathogen dynamics. Although this moderate level of explanatory power does not capture all variance, it remains significant given the inherent complexity of the ecological interactions that influence pathogen spread and survival. These values suggest that additional, unidentified factors likely play substantial roles; nevertheless, the environmental variables identified by us still provide crucial insights into pathogen distribution patterns. Such understanding is of vital importance to develop more targeted and effective environmental and public health interventions. Notably, these correlations did not establish definitive causal relationships or detailed mechanisms. Our findings provide valuable insights into the potential influence of air pollution (PM2.5, PM10, NO_2, and O_3) and ambient temperature on the prevalence of specific pathogens in hospitalized pediatric and women patients. Further empirical research is needed to validate these associations and gain a deeper understanding of the complex relationships between pathogens and environmental factors.

Although this study provides insightful data on the epidemiology of bacterial pathogens and their correlation with environmental factors, it has several limitations that should be considered when interpreting the results. First, as a single-center study, the findings may not fully represent the broader population, particularly since the hospital's catchment area is primarily Wuhan. Second, a minority of patients were from areas near Wuhan, but the environmental data collected did not comprehensively cover these regions. Therefore, the associations identified between pathogen prevalence and environmental factors may contain certain inaccuracies and thus not fully reflect the actual conditions experienced by these specific patients. In the future, multi-center studies are warranted to address these limitations and provide a more comprehensive understanding of the pathogens' epidemiology and their environmental interactions. This would expand the geographic and demographic diversity of the patient samples, thus enhancing the representativeness and accuracy of the findings. In addition, precise environmental mapping of patients' locations would be beneficial to draw a more accurate correlation between environmental exposures and pathogen prevalence.

Conclusion and Recommendation

This study underscores the significant variability in the distribution and antibiotic resistance of bacterial pathogens in Wuhan, accentuating the impact of local environmental factors. Importantly, *H. influenzae* and *S. pneumoniae* were found to primarily affect children under 6 years of age, highlighting the urgent need for targeted public health measures, including the integration of Hib and PCV13 vaccines into China's national immunization schedule to potentially reduce the disease burden substantially. Effective first-line treatments identified include ceftriaxone for ampicillin-resistant *H. influenzae*, penicillin G for *S. pneumoniae*, and cefotetan for *E. coli*. The prevalence of multidrug-resistant organisms remains below national averages, suggesting effective local healthcare strategies; however, continued vigilance remains necessary. Seasonal trends show *H. influenzae* peaking in late winter and early spring, whereas *M. catarrhalis* and *S. pneumoniae* peak in late summer to early autumn. Environmental factors, such as PM2.5 and PM10, are positively correlated with the increased detection of *H. influenzae, S. pneumoniae*, and *K. pneumoniae*, whereas NO2 is linked to increases in *S. aureus* and *M. catarrhalis*. Conversely, a negative correlation was observed between *E. coli* counts and ozone levels. This research advocates for extensive studies across multiple regions to develop comprehensive strategies that address pathogen behavior under diverse environmental influences, thus enhancing global public health responses, particularly in light of the challenges posed by global events like the COVID-19 pandemic.

Ethical Approval Statement

We confirm that our study strictly followed all ethical standards set forth in the Declaration of Helsinki. The study protocol was approved by the Ethics Review Committee of Wuhan Children's Hospital. Given the retrospective design of this study, it did not interfere with standard medical care or infringe on patient rights, and it did not pose any additional risk to participants. We ensured that patient identities were protected through coding, and medical records were securely stored and accessible only to researchers. The results are to be published as anonymous, aggregated data.

Funding

This study was supported by the National Natural Science Foundation of China (Grant No. 82072351), Wuhan Municipal Health Commission of China for the scientific research project WX20C10, and Wuhan Municipal Health Youth Talent Training Program (2021).

Disclosure

The authors declare that they have no known competing financial interests or personal relationships that could influence the work reported in this study.

References

1. Centers for disease control and prevention. bacterial infections. Available from: https://www.cdc.gov/antibiotic-use/community/about/antibiotic-resistance-faq.html. Accessed April 15, 2022.
2. World Health Organization. *Global Antimicrobial Resistance Surveillance System (GLASS) Report: Early Implementation 201–-2017*. Geneva, Switzerland: WHO Press; 2017.
3. World Health Organization. Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics; 2017. Available from: https://www.who.int/medicines/publications/global-priority-list-antibiotic-resistant-bacteria/en/. Accessed May 29, 2024.
4. David MZ, Daum RS. Community-associated methicillin-resistant Staphylococcus aureus: epidemiology and clinical consequences of an emerging epidemic. *Clin Microbiol Rev*. 2010;23:616–687. doi:10.1128/CMR.00081-09
5. Tangden T, Giske CG. Global dissemination of extensively drug-resistant carbapenemase-producing Enterobacteriaceae: clinical perspectives on detection, treatment and infection control. *J Intern Med*. 2015;277:501–512. doi:10.1111/joim.12342
6. Fouladkhah AC, Thompson B, Camp JS. The threat of antibiotic resistance in changing climate. *Microorganisms*. 2020;8. doi:10.3390/microorganisms8050748
7. Lei C, Lou CT, Io K, et al. Viral etiology among children hospitalized for acute respiratory tract infections and its association with meteorological factors and air pollutants: a time-series study (2014–2017) in Macao. *BMC Infect Dis*. 2022;22:588. doi:10.1186/s12879-022-07585-y
8. Liu WK, Chen DH, Tan WP, et al. Paramyxoviruses respiratory syncytial virus, parainfluenza virus, and human metapneumovirus infection in pediatric hospitalized patients and climate correlation in a subtropical region of southern China: a 7-year survey. *Eur J Clin Microbiol Infect Dis*. 2019;38:2355–2364. doi:10.1007/s10096-019-03693-x
9. Gona PN, More AF. Bacterial pathogens and climate change. *Lancet*. 2022;400:2161–2163. doi:10.1016/S0140-6736(22)02424-2
10. Humphries R, Bobenchik AM, Hindler JA, et al. Overview of changes to the clinical and laboratory standards institute performance standards for antimicrobial susceptibility testing, M100, 31st Edition. *J Clin Microbiol*. 2021;59:e0021321. doi:10.1128/JCM.00213-21
11. Liu Y, Wang W, Guo M, et al. The analysis of drug-resistant bacteria from different Regions of Anhui in 2021. *Infect Drug Resist*. 2022;15:7537–7553. doi:10.2147/IDR.S393760
12. Million Y, Feleke T, Mengesha D, et al. Multidrug-resistant bacteria among culture isolates at university of Gondar, specialized referral hospital, Northwest Ethiopia: a five-year retrospective study. *Clin Lab*. 2020;66. doi:10.7754/Clin.Lab.2019.190941
13. Chanda W, Manyepa M, Chikwanda E, et al. Evaluation of antibiotic susceptibility patterns of pathogens isolated from routine laboratory specimens at Ndola teaching hospital: a retrospective study. *PLoS One*. 2019;14:e0226676. doi:10.1371/journal.pone.0226676
14. Sharek PJ, Benitz WE, Abel NJ, et al. Effect of an evidence-based hand washing policy on hand washing rates and false-positive coagulase negative staphylococcus blood and cerebrospinal fluid culture rates in a level III NICU. *J Perinatol*. 2002;22:137–143. doi:10.1038/sj.jp.7210661
15. Yang Y, Wang Y, Yang D, et al. Factors associated with uptake of Haemophilus influenzae type b vaccination in Shanghai, China. *BMC Pediatr*. 2019;19. doi:10.1186/s12887-018-1374-6
16. Wang J, Qiu L, Bai S, et al. Prevalence and serotype distribution of nasopharyngeal carriage of Streptococcus pneumoniae among healthy children under 5 years of age in Hainan Province, China. *Infect Dis Poverty*. 2024;13. doi:10.1186/s40249-024-01175-7
17. Wang HJ, Wang CQ, Hua CZ, et al. Antibiotic resistance profiles of Haemophilus influenzae isolates from children in 2016: a multicenter study in China. *Can J Infect Dis Med Microbiol*. 2019;2019:6456321. doi:10.1155/2019/6456321
18. Vaez H, Sahebkar A, Pourfarzi F, et al. Prevalence of antibiotic resistance of Haemophilus influenzae in Iran- A meta-analysis. *Iran J Otorhinolaryngol*. 2019;31:349–357. doi:10.22038/ijorl.2019.34363.2137
19. Zhou M, Fu P, Fang C, et al. Antimicrobial resistance of Haemophilus influenzae isolates from pediatric hospitals in Mainland China: report from the ISPED program, 2017–2019. *Indian J Med Microbiol*. 2021;39:434–438. doi:10.1016/j.ijmmb.2021.09.001
20. Zhao C, Li Z, Zhang F, et al. Serotype distribution and antibiotic resistance of Streptococcus pneumoniae isolates from 17 Chinese cities from 2011 to 2016. *BMC Infect Dis*. 2017;17:804. doi:10.1186/s12879-017-2880-0
21. Stewart AG, Cottrell K, Henderson A, et al. In vitro activity of cefotetan against ESBL-producing Escherichia coli and Klebsiella pneumoniae bloodstream isolates from the MERINO trial. *Microbiol Spectr*. 2021;9:e0022621. doi:10.1128/Spectrum.00226-21
22. Xu J, Zhang Y, Ma H, et al. Analysis of factors related to neonatal infection and monitoring of bacterial drug resistance. *Z Geburtshilfe Neonatol*. 2022;226:399–404. doi:10.1055/a-1850-2475
23. Hu F, Guo Y, Yang Y, et al. Resistance reported from China antimicrobial surveillance network (CHINET) in 2018. *Eur J Clin Microbiol Infect Dis*. 2019;38:2275–2281. doi:10.1007/s10096-019-03673-1
24. Liu Y, Wang Q, Zhao C, et al. Prospective multi-center evaluation on risk factors, clinical characteristics and outcomes due to carbapenem resistance in Acinetobacter baumannii complex bacteraemia: experience from the Chinese Antimicrobial Resistance Surveillance of Nosocomial Infections (CARES) Network. *J Med Microbiol*. 2020;69:949–959. doi:10.1099/jmm.0.001222
25. Babu Rajendran N, Mutters NT, Marasca G, et al. Mandatory surveillance and outbreaks reporting of the WHO priority pathogens for research & discovery of new antibiotics in European countries. *Clin Microbiol Infect*. 2020;26:943 e941–943 e946. doi:10.1016/j.cmi.2019.11.020
26. Zhi-min GS-DHC-ZLJ-PCX-JSS-QC. Analysis on antibiotic resistance patterns and epidemiological features of 546 Haemophilus influenzae strains isolated from children during 2007–2014 in Children's Hospital. *Chin J Pract Pediatr*. 2016;2016(12):915–919.
27. Hu J, Wang XL, Xu F, et al. 流感嗜血杆菌阳性住院患儿回顾性流行病学调查 [Epidemiological survey of Haemophilus influenzae-positive hospitalized children: a retrospective analysis]. *Zhongguo Dang Dai Er Ke Za Zhi*. 2015;17:596–601. Chinese.
28. Huang F, Gu WJ, Jiang WJ, et al. 苏州地区流感嗜血杆菌感染与环境气候的相关因素分析 [Association of Haemophilus influenzae infection with environmental and climatic factors in Suzhou, China]. *Zhongguo Dang Dai Er Ke Za Zhi*. 2022;24:1351–1355. Chinese. doi:10.7499/j.issn.1008-8830.2205051