

Respiratory pathogen spectrum and coinfection patterns in acute respiratory infection patients during and post-COVID-19 pandemic from 2021 to 2025

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Abstract

Background

The coronavirus disease 2019 (COVID-19) pandemic prompted the implementation of non-pharmaceutical interventions (NPIs) globally. China adopted strict containment measures and widespread vaccination to mitigate SARS-CoV-2 transmission and reduce associated morbidity and mortality. This study aimed to analyze the epidemiological characteristics of 13 common respiratory pathogens in hospitalized patients with acute respiratory infection (ARI) during the COVID-19 pandemic and after the adjustment of containment measures from 2021 to 2025.

Methods

A retrospective analysis was conducted on 9,674 patients with acute respiratory infection (ARI), all of whom were tested for 13 respiratory pathogens using fluorescence PCR-capillary electrophoresis.

Results

Lower respiratory tract infections (LRTIs) demonstrated a significantly higher prevalence and diagnostic yield than upper respiratory tract infections (URTIs) (LRTI vs. URTI: 54.67% vs. 45.33%, $p < 0.001$; pathogen detection rate: 55.57% vs. 15.44%, $p < 0.05$). *Mycoplasma pneumoniae* emerged as the leading pathogen in LRTIs (18.08%), whereas rhinovirus predominated in URTIs (5.12%). Temporally, stringently enforced NPIs suppressed ARI incidence and positivity rates through 2021–2022 (2021: 1,180 cases, 27.63%; 2022: 1,161 cases, 24.38%). Following the post-2023 policy relaxation, a pronounced epidemiological resurgence occurred, with case volumes escalating to 4,292 (positivity rate: 34.62%) and peaking in 2024 at 54.84% (1,871 cases), before subsiding to 1,170 cases (positivity rate: 42.31%) by 2025. Within the critical care subset ($n = 79$), Influenza A (51.90%) and rhinovirus (16.46%) constituted the primary viral drivers; notably, 91.14% of ICU cases exhibited bacterial co-infections, among which 51.90% involved multidrug-resistant or resistant strains.

Conclusions

Due to the implementation and easing of COVID-19 non-pharmaceutical interventions, respiratory pathogen infections from 2021 to 2025 exhibited a trend of initial suppression followed by resurgence, with a higher incidence of multiple infections in the lower respiratory tract. Severe lower respiratory tract infection cases frequently involved mixed infections with bacteria, drug-resistant bacteria, and fungi, increasing the difficulty of prevention, control, and treatment, and necessitating optimized management strategies.

1. Introduction

Acute Respiratory Infection (ARI) is one of the most common infectious diseases in clinical practice. According to the infection site, it can be divided into Upper Respiratory Tract Infection (URTI) and Lower Respiratory Tract Infection (LRTI). URTI is mostly manifested as mild symptoms such as rhinitis and pharyngitis, while LRTI (e.g., bronchitis, pneumonia) is often accompanied by more severe lung injury, which can easily progress to severe infection and require hospitalization. Particularly in the elderly and immunocompromised populations, the mortality rate is relatively high [1].

In recent years, the epidemic spectrum of respiratory pathogens has been constantly changing, and the incidence of coinfections (virus-virus, virus-bacteria, bacteria-fungus) has increased. Combined with the problem of drug-resistant bacteria caused by the abuse of antibacterial drugs, it has brought great challenges to the diagnosis and treatment of ARI [2]. The global outbreak of COVID-19, resulting from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first identified in late 2019. The World Health Organization later declared it a public health emergency of international concern on January 30, 2020, and recognized it as a pandemic on March 11, 2020 [3–4]. In response, various non-pharmaceutical interventions (NPIs)—such as mask-wearing, hand hygiene, isolation of cases, and vaccine rollout—were widely introduced [5]. In China, a dynamic zero-COVID strategy was enforced, which remained in effect until December 26, 2022, when the country transitioned to Class B management of COVID-19, leading to the restoration of routine social and economic activities [6]. These rigorous NPIs significantly suppressed the spread of SARS-CoV-2 [7–12]. Furthermore, such measures also reduced the transmission of other respiratory pathogens, such as influenza virus, respiratory syncytial virus, and adenovirus [12–15]. In addition, after the COVID-19 pandemic, fluctuations in population immune levels and adjustments to protective measures may further affect the transmission and infection characteristics of respiratory pathogens [16].

This study focused on patients with acute respiratory infections (ARI) admitted to during and post-COVID-19 pandemic from 2021 to 2025. It systematically analyzed the pathogen detection rates, types of infections, and epidemic trends among patients with upper respiratory tract infections (URTI) and lower respiratory tract infections (LRTI). Additionally, the study investigated the etiological features of severe cases in the intensive care unit (ICU) who were infected with the 13 targeted pathogens. The objective was to provide an evidence-based foundation for the precise regional diagnosis and treatment of ARI, the prevention and control of coinfections, and the management of drug-resistant bacteria.

2. Materials and Methods

2.1 Study Subjects

A retrospective analysis was performed on ARI patients admitted to Hebei General Hospital during the period from January 2021 to December 2025 [17]:
 URTI: presenting with upper respiratory symptoms such as nasal congestion, sore throat, and runny nose, with no abnormal lung imaging findings;
 LRTI: accompanied by lower respiratory symptoms such as cough, expectoration, and shortness of breath, with chest CT/MRI indicating pulmonary inflammatory changes. Meanwhile, patients admitted to the ICU due to severe LRTI were included as subjects for analysis.

Exclusion criteria: Non-infectious respiratory diseases (e.g., acute asthma exacerbation, pulmonary interstitial fibrosis); Incomplete clinical data or unqualified test specimens.

2.2 Specimen Collection and Pathogen Detection

Respiratory specimens were collected from all patients within 24 hours of admission (throat swabs for URTI patients, sputum specimens or bronchoalveolar lavage fluid for LRTI and ICU patients). The following methods were used for pathogen detection:

- Detection of 13 respiratory pathogens:

The detection process consists of two stages: first, total nucleic acids were extracted using the Nucleic Acid Extraction or Purification Kit (Ning Bo Health Gene Technologies Co., Ltd, cat. 1060167); second, 13 types of respiratory pathogens were detected via mPCR combined with capillary electrophoresis, employing the Respiratory Pathogen Multiplex Kit (Ning Bo Health Gene Technologies Co., Ltd, cat. 1060071). These 13 pathogens included Influenza A virus (FluA, covering subtypes H7N9, H1N1, H3N2, and H5N2; among them, the 2009 H1N1 strain is referred to as FluA-H1N1, and H3N2 as FluA-H3N2); Influenza B virus (FluB, including Victoria and Yamagata lineages); Parainfluenza virus (PIV, types I to IV); Adenovirus (ADV, serotypes B, C, and E); Rhinovirus (RVs); Metapneumovirus (MPV); Respiratory syncytial virus (RSV, subgroups A and B); Coronavirus (CoV, strains 229E, OC43, NL63, and HKU1); Mycoplasma pneumoniae (MP); Chlamydia; and Bocavirus (BoV). Patient demographic details (such as sampling time, clinical diagnosis, age, gender, and name) along with laboratory test results were retrieved from the Laboratory Information System (LIS) of Hebei General Hospital.

2.3 Bacterial and Fungal Culture and Identification

From January 1, 2021, to December 31, 2025, all patients admitted to the Intensive Care Unit (ICU) due to severe ARI underwent bacterial and fungal culture and identification. According to clinical diagnosis and treatment standards, sputum or bronchoalveolar lavage fluid samples were collected from the enrolled patients. Sputum samples must meet the criteria for qualified sputum (white blood cells > 25 per low-power field and epithelial cells < 10 per low-power field). All samples were subjected to pathogenic microorganism isolation and culture, drug sensitivity testing, and drug resistance analysis in accordance with standard operating procedures.

2.4 Statistical Methods

SPSS 26.0 software was used for data analysis. Count data were expressed as "number of cases (percentage %, positive rate %)", and the chi-square test was used for comparison between groups; measurement data (e.g., age, length of hospital stay) were expressed as "median (interquartile range,IQR)" or "mean ± standard deviation", and the Mann-Whitney U test or t-test was used for comparison between groups. a p-value < 0.05 was considered statistically significant.

3. Results

3.1 Basic Epidemiological Characteristics of ARI Patients

A total of 9,674 ARI patients who visited Hebei General Hospital from January 2021 to December 2025 were included in this study, including 5,629 males (58.19%) and 4,045 females (41.81%), with a male-to-female ratio of 1.39:1. There was no statistically significant difference in gender composition among different years (p > 0.05). The median age of the patients was 58 years, with a median age of 16 years in 2021, 25 years in 2022, 66 years in 2023, 60 years in 2024, and 64 years in 2025. Among them, there were 308 infants, 717 toddlers, 1,199 preschool children, 1,213 school-age children, 1,975 adults, and 4,135 elderly patients. A total of 3,616 patients had positive respiratory pathogen detection, including 2,076 males and 1,542 females, with a male-to-female ratio of 1.35:1. The median age of patients with positive respiratory pathogen detection was 11 years, with a median age of 4 years in 2021, 5 years in 2022, 33 years in 2023, 42 years in 2024, and 12 years in 2025.(see Table 1).

The number of ARI patients increased significantly from 1,180 cases in 2021 and 1,161 cases in 2022 (during the pandemic) to 4,292 cases in 2023 (after the relaxation of [NPIs]).This was followed by a marked decline in subsequent years, with cases dropping to 1,871 in 2024 and further to 1,170 in 2025, suggesting a return towards pre-pandemic baselines.

A similar trend was observed in the positive detection rate of respiratory pathogens. The rate was 27.63% in 2021 and 24.38% in 2022, rising to 34.62% in 2023 post-relaxation. Interestingly, the rate peaked at 54.84% in 2024 before decreasing to 42.31% in 2025.

3.2 General Characteristics of Pathogen Detection in URTI and LRTI Patients

Of the 9,674 ARI patients included, 4,385 (45.33%) were diagnosed with upper respiratory tract infection (URT) and 5,289 (54.67%) with lower respiratory tract infection (LRTI). The number of patients with LRTI was significantly higher than that with URTI. The male-to-female ratio was 1.43:1 in the URTI group (2,580 males and 1,805 females) and 1.36:1 in the LRTI group (3,049 males and 2,240 females), with no statistically significant difference in gender composition between the two groups (p > 0.05).

Age distribution: The number of cases and positive detection rates of URTI and LRTI patients in each age subgroup (infants < 1 year old, toddlers 1 ~ < 3 years old, preschool children 3 ~ < 6 years old, school-age children 6 ~ < 14 years old, adults 14 ~ < 60 years old, elderly ≥ 60 years old) are shown in Table 1. Among

them, school-age children with LRTI had the highest pathogen positive detection rate (85.70%), followed by preschool children (79.59%).

A total of 3,881 strains of respiratory pathogens were detected in 9,674 ARI patients, involving 3,616 patients (positive detection rate: 37.38%). Among them, the positive detection rate in the LRTI group (55.57%) was significantly higher than that in the URTI group (15.44%) ($p < 0.001$), and statistically significant differences were observed in the detection rates of males, females, and all age subgroups (all $p < 0.05$) (see Table 1).

Table 1
Epidemiological characteristics of patients with URTI and LRTI

		URTI		LRTI		Total	
		Number	Positive n (%)	Number	Positive n (%)	Number	Positive n (%)
Total		4385	677(15.44)	5289	2939(55.57)	9674	3616(37.38)
Gender	Male	2580	384(14.88)	3049	1692(55.49)	5629	2076(36.88)
	Female	1805	293(16.23)	2240	1249(55.76)	4045	1542(32.55)
Age Group	Infants (< 1 year)	131	22(16.79)	177	145(81.92)	308	167(54.22)
	Toddlers (1 ~ < 3 years)	361	118(32.69)	356	270(75.84)	717	388(54.11)
	Preschool children (3 ~ < 6 years)	464	171(36.85)	735	585(79.59)	1199	756(63.05)
	School-age children (6 ~ < 14 years)	452	146(32.30)	888	761(85.70)	1213	907(74.77)
	Adults (14 ~ < 60 years)	901	101(11.21)	1074	465(43.30)	1975	566(28.66)
	Elderly (≥ 60 years)	2076	119(5.73)	2059	713(34.63)	4135	832(20.12)

Note: Numbers in the table represent the number of cases with ARTI; n (%) in the table represent the number of positive cases (positive detection rate)

3.3 Distribution of Infection Types and Composition of Main Pathogens in URTI and LRTI Patients

There were significant differences in the distribution of infection types (single infection, double infection, triple infection) between URTI and LRTI patients ($p < 0.001$), as detailed below (Table 2):

URTI group: dominated by single infection (14.66%, 643/4385), with double infection accounting for 1.55% (68/4385) and triple infection accounting for only 0.11% (5/4385);

LRTI group: single infection accounted for 52.14% (2758/5289), double infection accounted for 7.24% (383/5289), and triple infection accounted for 0.85% (45/5289);

The rate of multiple infections (double + triple infections) in the LRTI group (8.09%) was significantly higher than that in the URTI group (1.66%) ($p < 0.001$).

There were significant differences in the dominant pathogens between URTI and LRTI patients, and the detection rate of all pathogens in the LRTI group was significantly higher than that in the URTI group (all $p < 0.05$) (Table 2, Fig. 1):

URTI group: the top 5 pathogens in terms of detection rate were RVs (4.12%), FluA (4.1%), ADV (2.42%), PIV (1.21%), and Cov (1.07%);

LRTI group: the top 5 pathogens in terms of detection rate were MP (18.08%), RVs (11.72%), FluA (8.75%), RSV(6.05%), and ADV (4.59%) ;

Among them, the detection rate of MP in LRTI (15.73%) was more than 27 times that in URTI, and the detection rate of FluA in LRTI was 2.1 times that in URTI.

Table 2
Type of infection and detection of respiratory pathogens in URTI and LRTI patients

Single infection	URTl Positive n (%)	LRTl Positive n (%)	Total Positive n (%)
	643(14.66)	2758(52.14)	3401(35.16)
Double infection	68(1.55)	383(7.24)	165(2.49)
Triple infection	5(0.11)	45(0.85)	50(0.52)
Influenza A virus (FluA)	180 (4.1)	463 (8.75)	643(6.65)
Influenza B virus (FluB)	31 (0.71)	79 (1.49)	110(1.14)
Parainfluenza virus (PIV)	53 (1.21)	228 (2.91)	281 (2.90)
Adenovirus (ADV)	106 (2.42)	243 (4.59)	349 (3.61)
Rhinovirus (RVs)	227 (5.12)	620 (11.72)	847(8.76)
Metapneumovirus (MPV)	29 (0.66)	215 (4.07)	244 (2.52)
Respiratory syncytial virus (RSV)	25 (0.57)	320 (6.05)	345 (3.57)
Coronavirus (CoV)	47 (1.07)	80 (1.51)	127 (1.31)
Mycoplasma pneumoniae (MP)	29 (0.66)	956 (18.08)	985 (10.18)
Chlamydia	4 (0.09)	32 (0.61)	36 (0.37)
Bocavirus (BoV)	18 (0.41)	58 (1.10)	76(0.79)
Total	677(15.44)	2939(55.57)	3616(37.38)
Note: n (%) in the table represent the number of positive cases (positive detection rate)			

3.4 Hospitalization Status and Annual Trend of Positive Patients

Among the 3,616 pathogen-positive patients, 97.65% were inpatients (3,531/3,616), of whom LRTI accounted for 82.5% (2,913/3,531). Annual trend analysis showed that the number of positive ARI inpatients in 2023 (1,407 cases) and 2024(1,021 cases) was significantly higher than that in 2021 (324 cases) and 2022 (279 cases) ($p < 0.05$),with a notable decrease to 585 cases in 2025..

Furthermore, the rate of multiple infections in LRTI inpatients exhibited an overall increasing trend from 2021 to 2024, followed by a slight decrease in 2025: 3.94% (8/203) in 2021, 6.42% (14/218) in 2022, 10.83% (123/1,135) in 2023, 11.65% (235/2,018) in 2024, and 9.93% (106/1,068) in 2025. The rates in 2023, 2024 and 2025 were all significantly higher than those recorded in 2021 and 2022 (all $p < 0.05$).

3.5 Clinical and Etiological Characteristics of ICU Patients with Severe LRTI

3.5.1 Basic Information

Of the 9,674 patients included in the study, 79 (0.82%) were admitted to the Intensive Care Unit (ICU) due to severe lower respiratory tract infection (LRTI). The annual distribution of these severe cases was as follows: 2 cases in 2021, none in 2022, and a notable increase to 44 cases in 2023, followed by 23 cases in 2024, and 10 cases in 2025.

The demographic profile of the ICU-admitted patients was characterized by a male predominance, with 58 males (73.42%) and 21 females (26.58%). The age of these patients ranged from 27 to 97 years, with a median age of 69 years (interquartile range,IQR: 65–76). Elderly individuals aged over 60 years constituted the majority of this cohort, accounting for 62.03% (49/79) of the severe cases.

3.5.2 Characteristics of Pathogen Detection and Spectrum of Co-infections in ICU Patients

Of the 9,674 patients with acute respiratory infection (ARI), 79 required admission to the intensive care unit (ICU). Among these critically ill patients, 11 (13.92%) had no underlying diseases. The remaining 68 patients (86.08%) had at least one underlying condition, including cerebral infarction (9 cases), cerebral hemorrhage (5 cases), epilepsy (2 cases), other neurological disorders (7 cases), cardiovascular diseases (10 cases), renal diseases (5 cases), diabetes with complications (2 cases), malignancy (3 cases), fractures or trauma (4 cases), chronic obstructive pulmonary disease or interstitial lung disease (7 cases), and other comorbidities (14 cases).

At least one of the 13 Respiratory pathogens was detected in all 79 patients. Respiratory pathogen infections were predominantly single infections, accounting for 76 cases (96.20%), while only 3 cases (3.80%) presented as dual infections—specifically, 1 case of FluA-H3N2 + ADV, 1 case of FluB + RSV and 1 case of ADV + BoV. FluA emerged as the most frequently detected pathogen, accounting for 51.90% (41/79) of all cases, with the H3N2 subtype (22 cases) showing a comparable prevalence to the H1N1 subtype (19 cases). RVs (16.46%, 13/79) and ADV (7.59%, 6/79) were also frequently detected. In addition, 6 cases of FluB, 3 cases of PIV, 3 cases of MPV, 2 cases of RSV, 1 case of BoV, and 1 case of CoV were also detected.

Of the 72 patients with concurrent bacterial or fungal co-infections, the distribution of major respiratory viruses and their corresponding co-infecting pathogens was characterized as follows: FluA-H3N2 (22 cases) was most frequently co-infected with AB (11 cases, including 7 cases of CRAB), KP (7 cases, including 3 cases of CRE), and PA (4 cases). Nine of these patients were co-infected with two or more bacterial species. FluA-H1N1 (19 cases) was commonly co-infected with AB (10 cases, including 8 cases of CRAB), KP (8 cases, including 4 cases of CRE), PA (1 case), and AF (1 case). Seven patients in this group had polymicrobial infections involving at least two pathogens. RVs (13 cases) were predominantly co-infected with AB (5 cases, all CRAB), KP (5 cases, including 4 CRE), and PA (2 cases). ADV (6 cases) was mainly co-infected with KP (3 cases), AB (3 cases), and BC (1 case).

The spectrum of bacterial co-infections was dominated by AB (40 cases), KP (31 cases), and PA (13 cases); SM was identified in 4 cases. A high proportion of patients (59.49%, 47/79) were infected with two or more bacterial species. Drug-resistant strains were isolated from 51.90% (41/79) of patients, primarily comprising CRAB (27 cases) and CRE (13 cases). One case each of MRSA and MRSCN were also identified. Co-infection with both CRAB and CRE was observed in 9 patients. Fungal infections were present in 16.46% (13/79) of cases, predominantly involving *Candida* species (4 *C. albicans*, 3 *C. tropicalis*, and 1 *C. glabrata*), followed by AF (4 cases) and HC (1 case).

3.5.3 Death Cases and Length of Hospital Stay

The mortality rate was 8.86% (7/79). These fatal cases had a mean age of 85 years, with only one female case and the rest being male cases; all of them were diagnosed with virus-bacteria mixed infections. The specific pathogen combinations were as follows: RVs+*Proteus mirabilis* + PA + *Serratia marcescens*; CoV + *Citrobacter braakii*; FluA-H1N1 + PA+*Elizabethkingia meningoseptica*+*Delftia acidovorans*; FluA-H3N2 + *Candida* spp; FluA-H1N1 + *Staphylococcus aureus* + KP; FluA-H1N + AB+*Staphylococcus aureus*; FluA + AB+*Stenotrophomonas maltophilia*+*Klebsiella oxytoca*.

The hospital length of stay for patients ranged from 2 to 56 days, with a median of 15 days and a mean of 19 days. Statistical analysis revealed that the mean hospital stay was significantly longer in patients with concurrent multidrug-resistant bacterial infections (26 days) compared to those with infections caused by susceptible bacteria (19 days) ($p < 0.05$). Similarly, patients with concurrent fungal infections had a significantly prolonged mean length of stay (25 days) relative to those without fungal infections (17 days) ($p < 0.05$).

4. Discussion

Based on the cohort of ARI patients in Hebei General Hospital from 2021 to 2025, this study systematically analyzed the pathogen characteristics of URTI and LRTI patients and the clinical rules of the ICU severe subgroup for the first time. The core findings and clinical significance are as follows:

4.1 Clinical Significance of Differences in Pathogen Detection Between URTI and LRTI

The pathogen detection rate of LRTI patients (55.57%) was significantly higher than that of URTI patients (15.44%). This result is closely related to the pathophysiological characteristics of LRTI: LRTI is often accompanied by alveolar epithelial injury and increased mucus secretion, which enhances the colonization and replication ability of pathogens in the lungs. In contrast, URTI is mostly limited to the surface of the upper respiratory mucosa with low pathogen load, leading to the difference in detection rate [18]. In addition, school-age children LRTI patients had the highest positive rate (85.70%), suggesting that priority should be given to improving etiological detection for school-age children LRTI to guide precise medication.

There were significant differences in dominant pathogens between URTI and LRTI: URTI was dominated by RVs and FluA [19]; while MP had the highest detection rate (18.08%) in LRTI, which is consistent with the recent epidemic trend of drug-resistant MP strains (especially macrolide-resistant strains) in China. MP evades the action of antibiotics through 23S rRNA gene mutation, leading to prolonged infection and easy progression to LRTI [20]. In addition, the high detection rate of FluA in LRTI (8.75%), FluA may directly damage the alveolar epithelial barrier and promote secondary bacterial infections (e.g., KP, AB) [21].

4.2 Epidemic Trend of Coinfections and Prevention Challenges

This study found that the rate of multiple infections in LRTI patients (7.47%) was significantly higher than that in URTI patients (1.66%), and the rate of multiple infections in LRTI inpatients in 2023 (10.83%) increased significantly compared with 2021–2022, while it plateaued in 2024 (10.49%), remaining essentially at the high level observed in 2023. This trend may be related to changes in population immune status after the COVID-19 pandemic: during the pandemic, measures such as mask-wearing and social distancing significantly reduced the transmission of common respiratory viruses, but also weakened the population's immune memory to non-COVID-19 viruses (e.g., FluA, RVs); after the relaxation of prevention and control measures in 2023, virus transmission resumed, combined with the prevalence of drug-resistant MP strains, which jointly increased the risk of coinfections [22]. Upon entering 2024, as the epidemic rhythms of major infectious diseases gradually returned to pre-pandemic patterns and population immune barriers were potentially strengthened, the infection rate stabilized into a steady plateau.

It is worth noting that the main modes of multiple infections in LRTI were "RVs + MP" (61 cases) and "FluA + ADV" (16 cases). Such combinations may aggravate lung injury through synergistic effects: for example, RVs can damage the integrity of the respiratory mucosa and promote MP adhesion and colonization; FluA can inhibit the function of host immune cells and increase the replication efficiency of ADV. Therefore, clinicians should be alert to the possibility of multiple infections in LRTI patients, especially in the elderly and immunocompromised populations. It is recommended to use multi-pathogen combined detection technologies (e.g., mPCR) to improve the detection rate [23].

4.3 Diagnosis and Treatment Difficulties and Management Strategies for ICU Severe LRTI Patients

Notably, among hospitalized patients with pathogen-confirmed LRTI, the ICU admission rate exhibited a sharp rise from 0% in 2022 to 3.13% in 2023, followed by a gradual decline to 2.25% in 2024 and 1.71% in 2025. This trend strongly suggests that prolonged and stringent non-pharmaceutical interventions may have led to a decline in population-level immune defenses against common respiratory pathogens—a phenomenon known as "immunity debt"—which not only resulted in a surge of infections after the relaxation of restrictions but also significantly increased the risk of progression to severe disease. Although the gradual accumulation of natural infections contributed to immune restoration during 2024–2025, leading to a decrease in severe cases, ICU admission rates have not yet fully returned to pre-pandemic levels, highlighting the need for sustained vigilance regarding severe LRTI in the post-pandemic era.

In line with this heightened risk, ICU severe LRTI patients showed the characteristics of "advanced age, high comorbidity rate, and high drug-resistant bacterial infection rate": 62.03% were elderly patients over 60 years old, 86.08% had underlying diseases, 91.14% had concurrent bacterial infections, and 51.90% had drug-resistant strains detected, which is consistent with the epidemiological characteristics of global ICU infections [24]. Among them, 59.49% of ICU patients had concurrent infections with ≥ 2 types of bacteria, and 9 cases were infected with both CRAB and CRE. Such multidrug-resistant bacteria are resistant to most antibacterial drugs, leading to limited treatment options and increased medical burden. The length of hospital stay of patients with coinfections (average 26 days) was significantly longer than that of patients without drug-resistant bacterial infections (19 days).

The high-risk factors for drug-resistant bacterial infections can be summarized into three points: ①Antibiotic selection pressure: the widespread use of carbapenem antibiotics such as meropenem promotes the prevalence of drug-resistant bacteria by inducing horizontal transfer of drug-resistant genes (e.g., blaKPC, blaOXA-23); ②Medical device-related infections: equipment such as ventilator circuits and central venous catheters provide carriers for biofilm formation of AB, leading to persistent infections [25]; ③Immunosenescence: the decline of T cell function and neutrophil phagocytosis in elderly patients makes it impossible to effectively clear pathogens, prolonging the infection course [26].

In addition, the 16.43% fungal infection rate in ICU patients also requires vigilance: mainly *Candida* (*Candida albicans*, *Candida tropicalis*). The length of hospital stay of patients with concurrent fungal infections (average 25 days) was significantly longer than that of patients without fungal infections (17 days). The use of broad-spectrum antibiotics disrupts the balance of intestinal flora, leading to the translocation of opportunistic pathogens such as *Candida* to the respiratory tract [27]; at the same time, the use of glucocorticoids and immunosuppressants inhibits the Th1-type immune response and reduces the secretion of antifungal cytokines (e.g., IFN- γ), further increasing the risk of fungal infections [28]. One death case in this study was "FluA-H3N2 + *Candida* spp. infection", suggesting that fungus-virus synergistic infection may aggravate the condition [29]. Clinicians should carry out early fungal detection (e.g., G test, fungal culture).

4.4 Study Limitations and Future Directions

This study has the following limitations: ①It is a single-center retrospective study, and the samples may have regional bias; ②Pathogen detection did not cover all pathogens, which may lead to missed detection;

Future studies can conduct multi-center, prospective cohort studies, include ARI patients from more regions, and improve the pathogen spectrum using technologies such as mNGS.

5. Conclusions

This five-year retrospective study revealed significant epidemiological shifts in acute respiratory infections (ARI) among patients at Hebei General Hospital from 2021 to 2025. Throughout the study period, lower respiratory tract infections (LRTI) were consistently more prevalent than upper respiratory tract infections (URTI), with LRTI patients exhibiting significantly higher pathogen detection rates and greater risks of multiple infections. *Mycoplasma pneumoniae* and influenza A virus were identified as the dominant pathogens in LRTI.

Notably, the post-pandemic relaxation of containment measures in 2023 triggered a dramatic surge in both ARI cases and pathogen positivity rates, which peaked during that year before substantially declining in 2024 and 2025. Concurrently, the rate of multiple infections among hospitalized LRTI patients increased significantly in 2023 compared to 2021–2022, intensifying prevention and control challenges, and has since plateaued at elevated levels.

Severe LRTI cases requiring ICU admission were predominantly elderly males, characterized by high rates of bacterial, drug-resistant bacterial, and fungal co-infections. Multidrug-resistant organisms and fungal infections were significantly associated with prolonged hospital stays, while advanced age and mixed infections emerged as key risk factors for mortality. Although the overall disease burden has receded from its 2023 peak, the persistently elevated rates of multiple infections and ICU admissions underscore the need for continued vigilance.

The findings of this study provide important evidence-based references for the precise clinical diagnosis and treatment of ARI—particularly LRTI—as well as for the prevention and control of co-infections and the management of drug-resistant bacteria in the post-pandemic era.

Declarations

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Ethics approval and consent to participate: This study was conducted in strict accordance with the Declaration of Helsinki. This study has been approved by the Medical Ethics Committee of Hebei General Hospital [No. 2024-LW-0210]. As a retrospective study using anonymized routine clinical and laboratory data collected during standard medical care, the Ethics Committee granted a waiver of informed consent for participation. No new interventions or samples were obtained, and all data were analyzed anonymously with strict protection of patient privacy.

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Data Availability Statements: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Figures

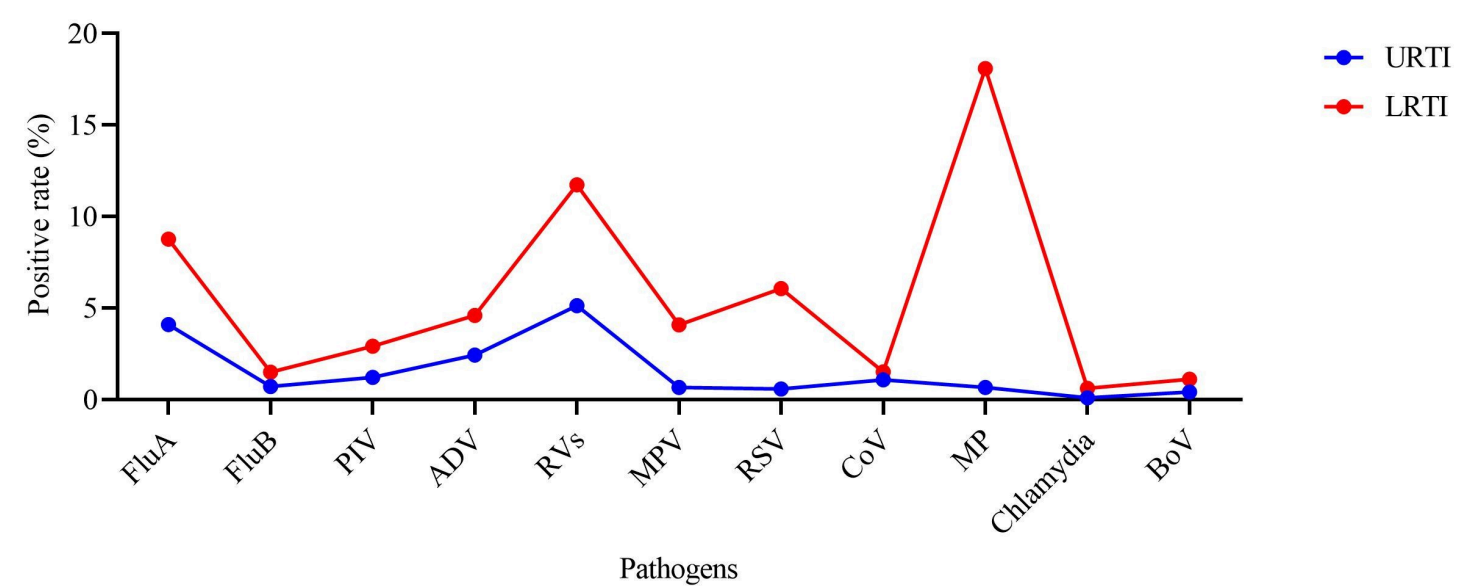


Figure 1

Detection of respiratory pathogens in URTI and LRTI patients