BMC Infectious Diseases

RESEARCH

Open Access

Factors affecting the severity of respiratory infections: a hospital-based cross-sectional study

Yunshao Xu[1†], Li Qi[2†], Jule Yang[2], Yuping Duan[1], Mingyue Jiang[1], Yanxia Sun[1], Yanlin Cao[1], Zeni Wu[1*], Wenge Tang[2*] and Luzhao Feng[1*]

Abstract

Background Acute respiratory infections (ARIs) are a leading cause of global morbidity and mortality, with disease severity influenced by factors such as advanced age, underlying comorbidities, and pathogen type. This report analyzed the association between several clinical variables and disease severity.

Methods A hospital-based cross-sectional study was conducted from September 2023 to April 2024, with data collected from eight districts in Chongqing, China. The study included 1,638 patients with ARIs, including both severe and mild cases. Severe cases were identified using the qSOFA and APACHE II scores, while demographic and clinical data were obtained via questionnaires and hospital records. Pathogen detection was performed using real-time quantitative PCR. Data analysis was carried out using Stata 17.0, with multiple logistic regression models assessing the associations between clinical factors and disease severity.

Results Influenza A was the most prevalent pathogen, detected in 65.1% of severe cases and 32.9% of mild cases ($P < 0.001$). 42.0% (165/393) of severe cases had viral and bacterial co-infections, compared to 26.8% (334/1,245) of mild cases ($P < 0.001$). The most common pathogens in co-infections included influenza A and *Streptococcus pneumoniae*. Severe cases were more common in rural areas (28.8% vs. 18.1%, $P < 0.001$) and among older adults (≥ 60 years) (28.2% vs. 13.5%, $P < 0.001$). Clinical symptoms such as fever (61.8% vs. 40.9%, $P < 0.001$), cough (68.7% vs. 53.2%, $P < 0.001$), and dyspnea (34.8% vs. 15.1%, $P < 0.001$) were significantly more prevalent in severe cases. Logistic regression analysis showed that influenza A (OR: 4.52, 95% CI: 3.51–5.85), *Streptococcus pneumoniae* (OR: 1.54, 95% CI: 1.28–2.15), and pre-existing cardiovascular diseases (OR: 1.96, 95% CI: 1.28–2.99) were significantly associated with the development of severe outcomes.

†Yunshao Xu and Li Qi have contributed equally to this work.

*Correspondence:
Zeni Wu
zeni.wu@pumc.edu.cn
Wenge Tang
690615630@qq.com
Luzhao Feng
fengluzhao@cams.cn

Full list of author information is available at the end of the article

Conclusions This study underscores the complex interplay of factors influencing ARI severity, including pathogen type, co-infections, age, and underlying medical conditions. Early identification of high-risk patients, particularly those with bacterial co-infections and cardiovascular comorbidities, is essential for improving clinical outcomes in ARI patients. Targeted treatment and preventative strategies are needed to mitigate severe disease in vulnerable populations.

Clinical trial number Not applicable.

Keywords Respiratory infections, Cross-sectional study, Severity

Background

Respiratory infections remain a leading global cause of morbidity and mortality, with significant variations in severity influenced by factors such as age, pre-existing conditions, and pathogen type [1]. Early identification of high-risk patients is critical for improving clinical outcomes, particularly in vulnerable populations such as older adults and those with chronic diseases [2–4]. Older age, pre-existing medical conditions, and specific viral infections, such as Influenza A and B, are associated with adverse outcomes [3, 4]. However, existing studies have been limited by their narrow focus on specific bacterial and viral pathogens, with insufficient attention given to the role of underlying diseases, complications, and co-infections in determining disease severity. Bacterial co-infections, such as *Streptococcus pneumoniae* and *Haemophilus influenzae*, exacerbate disease severity [2]. Age-related immune system decline, chronic comorbidities, and bacterial superinfections have all been identified as risk factors for severe outcomes [3, 4]. Clinical symptoms such as fever, cough, and dyspnea were strongly associated with disease severity, serving as key indicators for clinicians to identify high-risk patients. This study examined pneumonia, bronchitis, and severe cases defined by the APACHE II score as outcomes to explore the potential impact of patient age, underlying medical conditions, clinical symptoms, pathogen infections, and co-infections on the severity of acute respiratory infections.

Methods

Data were collected from eight districts in Chongqing, China (Fuling, Wanzhou, Qianjiang, Banan, Yongchuan, Nan'an, Jiangjin, and Xiushan) between September 2023 and April 2024. Patients from 23 medical institutions were enrolled, including departments of respiratory medicine, pediatrics, emergency care, and fever clinics. Severe cases of respiratory infections were randomly selected from patients requiring hospitalization for at least 24 h. The control group comprised age- and gender-matched patients (1:3) from the same time period who were treated as outpatients. This classification was further supported by clinical severity scores, including the APACHE II score, to ensure a more objective assessment of disease severity. Mild cases were defined as patients with a qSOFA score of ≤ 2. Severe cases were initially screened using the qSOFA score with a threshold of ≥ 3, and further assessed using the APACHE II score for confirmation. A specific cutoff for severe cases in APACHE II scoring was set at ≥ 10, corresponding to a higher risk of mortality and severe organ dysfunction, which is a commonly accepted threshold used in clinical practice. The diagnostic criteria for pneumonia and bronchitis in this study were determined by clinicians based on chest imaging results. A questionnaire was developed for this study and used to collect information on sex, age, body mass index (BMI), residential area, interval from onset to medical consultation, complications, preexisting conditions, smoking status, auxiliary treatment, course duration, and clinical outcomes. All questionnaires were reviewed by the attending physicians of the patients to ensure that the information provided was consistent with the data in the Hospital Information System. Social demographic and clinical information of patients obtained from follow-up visits. The ethical review of the project was done by the Ethics Committee of the Chongqing Center for Disease Control and Prevention, and informed consent was obtained from all relevant personnel.

Nucleic acid testing was conducted using real-time quantitative PCR (qPCR) on nasopharyngeal swab samples to detect 17 respiratory pathogens (*S. pneumoniae*, *H. influenzae*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Bordetella pertussis*, *Mycoplasma pneumoniae*, influenza A and B, rhinovirus, adenovirus, enterovirus, respiratory syncytial virus, human metapneumovirus, parainfluenza virus, coronavirus, and bokavirus). The test reagent was the Respiratory Pathogen Nucleic Acid Multiplex Test Kit from Jiangsu Hechuang Biotechnology Co. Primers were designed based on conserved regions of each pathogen, and reaction conditions were standardized to ensure reproducibility. Positive and negative controls were used to ensure the validity of the result. Data analysis was conducted using Stata 17.0 (StataCorp). The univariable analysis included chi-square tests. Multiple logistic regression models were used to assess the association between each clinical factor and disease severity after adjusting for confounding factors such as age groups, gender, BMI,

residential area, illness onset months, and smoking status. A two-sided $P < 0.05$ was considered significant.

Results

Overall, 1,638 patients with respiratory infections were included in this study, of whom 1,245 (76.1%) were classified as mild cases and 393 (23.9%) as severe cases. The distribution of cases across urban and rural areas was significantly different ($P < 0.01$), with a higher proportion of severe cases originating from rural regions. In total, 81.9% of mild cases (1,020/1,245) and 71.2% of severe cases (280/393) were from urban areas ($P < 0.01$); 18.1% of mild cases (225/1,245) and 28.8% of severe cases (113/393) were from rural areas ($P < 0.001$). Most patients had a normal BMI (62.7% of mild cases and 55.7% of severe cases). Younger patients (0–17 years) accounted for the highest proportions of mild (48.4%) and severe cases (42.5%). Older adults (≥ 60 years) accounted for 13.5% of mild cases and 28.2% of severe cases. Mild cases had a higher cure rate (45.0%) than severe cases (41.6%) (Table 1).

The most frequently detected respiratory pathogens were influenza A (40.6%), influenza B (19.4%), and *Haemophilus influenzae* (18.36%). Notably, influenza A was significantly more prevalent in severe cases (65.1%) compared to mild cases (32.9%, $P < 0.001$). Influenza A was the most prevalent among mild (32.9%) and severe cases (65.1%). *S. pneumoniae* and *P. aeruginosa* were detected in 14.8% and 9.7% of cases, respectively. *S. pneumoniae* was more common in severe cases (17.5%) than in mild cases (14.1%). Severe cases showed higher detection rates of bacterial co-infections, such as *P. aeruginosa* (12.2%), than mild cases (8.3%) (Table 2).

Among the 1,638 patients, 38.8% had viral infections, 9.8% had bacterial infections, and 30.5% had viral/bacterial co-infections. Severe cases were more likely to be associated with viral infections (53.9%) and had a higher proportion of co-infections (42.0%) than mild cases (26.8%). Mild cases were balanced between viral (33.9%) and co-infections (26.8%). Common symptoms, such as fever, cough, and sputum production, were prevalent across all groups, with co-infected patients showing higher frequencies than those with strictly viral or bacterial infections (Table 3).

The association between clinical information and disease severity is shown in Fig. 1 and Additional file 1 (Table S1-S3). The development of pneumonia was significantly associated with the following risk factors: individuals aged 60 years and above (odds ratio [OR]: 4.03, 95% confidence interval [CI]: 2.58–6.29), infection with respiratory syncytial virus (OR: 3.31, 95% CI: 1.60–6.87), influenza A(OR: 1.51, 95% CI: 1.10–2.07), and-influenza B (OR: 1.57, 95% CI: 1.09–2.26), as well as pre-existing lung diseases (OR: 2.34, 95% CI: 1.48–3.70) and cardiovascular diseases (OR: 2.62, 95% CI: 1.62–4.24). The development of bronchitis was significantly associated with the following risk factors: individuals aged 0–17 years (OR: 2.48, 95% CI: 1.55–3.97), infection with *S. pneumoniae* (OR: 1.73, 95% CI: 1.17–2.56), *P. aeruginosa* (OR: 1.99, 95% CI: 1.25–3.17), and influenza B (OR: 1.51, 95% CI: 1.04–2.20), as well as pre-existing lung diseases (OR: 1.71, 95% CI: 1.03–2.85). For those severe cases, fever (OR: 1.61, 95% CI: 1.21–2.14), cough (OR: 2.05, 95% CI: 1.49–2.82), dyspnea (OR: 1.95, 95% CI: 1.11–3.43), vomiting (OR: 2.19, 95% CI: 1.31–3.66) and Nausea (OR: 1.85, 95% CI: 1.06–3.23) were significantly associated with an increased risk of severe outcomes. However, other symptoms like muscle pain (OR: 1.07, 95% CI: 0.77–1.48) and sore throat (OR: 0.70, 95% CI: 0.54–0.92) did not show a significant association with severe outcomes. Detection of *S. pneumoniae* (OR: 1.54, 95% CI: 1.28–2.15), influenza A (OR: 4.52, 95% CI: 3.51–5.85), and influenza B (OR: 2.38, 95% CI: 1.81–3.13) significantly associated with severe outcomes. Patients with pre-existing cardiovascular diseases (OR: 1.96, 95% CI: 1.28–2.99) were more likely to experience severe outcomes.

The relationships between various respiratory pathogens and infection types are shown in Fig. 2 and Additional file 1 (Table S4). Among viral infections, Influenza A virus was positively correlated with the detection of bacterial ($r = 0.168$, $P < 0.01$). Influenza B virus and rhinovirus also exhibited positive associations, with correlation coefficients of 0.180 and 0.143, respectively (both $P < 0.01$). The remaining common viruses (adenovirus, enterovirus, respiratory syncytial virus, human metapneumovirus, parainfluenza virus, coronavirus, and bocavirus) showed correlation coefficients ranging from 0.057 to 0.114. Among bacterial infections, *S. pneumoniae* exhibited the most significant positive correlation with viral infections ($r = 0.448$, $P < 0.01$), followed by *H. influenzae* ($r = 0.264$, $P < 0.01$). *P. aeruginosa*, *S. aureus*, and *K. pneumoniae* showed correlation coefficients with viral infections of $P > 0.05$, which did not reach statistical significance. In virus-virus pairs, the negative correlation between Influenza A and Influenza B was the most significant ($r = -0.407$, $P < 0.01$), indicating that these two types of influenza viruses are less likely to be co-detected. Rhinovirus showed low to moderate positive correlations with enterovirus ($r = 0.149$, $P < 0.01$) and adenovirus ($r = 0.085$, $P < 0.01$). The overall correlation coefficients between virus-bacteria pairs were generally low ($r < 0.10$). However, most of the statistically significant correlations were positive. For example, a significant positive correlation was observed between Influenza B virus and Streptococcus pneumoniae ($r = 0.053$, $P < 0.05$).

Table 1 Social demographic and clinical information for patients with acute respiratory infections [N (%)]

Basic Information	Mild Cases	Severe Cases	*P*
Total Number	1245	393	
Gender			0.391
Male	609 (48.9)	202 (51.4)	
Female	636 (51.1)	191 (48.6)	
Age (years)			< 0.001
0–17	596 (48.4)	164 (42.5)	
18–59	469 (38.1)	113 (29.3)	
≥ 60	167 (13.5)	109 (28.2)	
BMI			0.015
Underweight	97 (7.8)	48 (12.2%)	
Normal	782 (62.7)	219 (55.7)	
Overweight	242 (19.4)	78 (19.8)	
Obese	124 (10.0)	48 (12.2)	
Residential Area			< 0.001
Urban	1020 (81.9)	280 (71.2)	
Rural	225 (18.1)	113 (28.8)	
Interval from Onset to Medical Consultation (days)			0.060
0–3	561 (78.1)	178 (75.1)	
4–7	76 (10.6)	38 (13.9)	
≥ 8	81 (11.3)	21 (9.9)	
Complications			
No Complications	1063 (84.6)	192 (46.7)	< 0.001
Bronchitis	106 (13.4)	63 (15.3)	0.420
Pneumonia	64 (5.1)	115 (30.0)	< 0.001
Other	24 (1.9)	41 (10.0)	< 0.001
Pre-existing Conditions			
No Pre-existing Conditions	555 (69.4)	125 (46.1)	< 0.001
Lung Diseases	100 (12.6)	56 (20.7)	0.020
Cardiovascular Diseases	66 (8.3)	51 (18.9)	< 0.001
Diabetes	31 (3.9)	20 (7.4)	0.030
Tumors	16 (2.0)	8 (3.0)	0.440
Other	32 (4.0)	11 (4.1)	0.900
Smoking Status			0.490
Non-smoker	551 (44.4)	181 (46.2)	
Long-term Smoker	152 (12.2)	57 (14.5)	
Occasional Smoker	504 (40.7)	142 (36.2)	
Former Smoker	32 (2.6)	12 (3.1)	
Auxiliary Treatment			< 0.001
Oxygen	45 (3.6)	38 (9.7)	
Not Used	1195 (96.4)	354 (90.3)	
Course Duration (days)			0.607
0–6	256 (60.2)	84 (64.6)	
7–13	159 (37.4)	41 (31.5)	
≥ 14	10 (2.4)	5 (3.8)	
Clinical Outcome			0.349
Cure	555 (45.0)	161 (41.6)	
Improvement	676 (54.9)	225 (58.1)	
Death	1 (0.1)	1 (0.3)	

Note: Descriptive statistics were utilized to summarize the demographic and clinical characteristics of the patients. Comparisons between severe and mild cases were performed using chi-square tests, with a *P*-value of < 0.05 considered statistically significant. BMI classification and Smoking Status are based on WHO standards, and Residential Area is based on actual current residence. BMI = Body Mass Index

Table 2 Test indicators and pathogen detection rates in mild and severe acute respiratory infections [N (%)]

Test Indicators	Total	Mild	Severe
Influenza A Virus	666 (40.6)	410 (32.9)	256 (65.1)
Influenza B Virus	319 (19.4)	202 (16.2)	117 (29.7)
Rhinovirus	74 (4.4)	70 (5.6)	4 (1.0)
Adenovirus	13 (0.8)	11 (0.8)	1 (0.2)
Enterovirus	28 (1.7)	26 (2.0)	3 (0.7)
Respiratory Syncytial Virus	40 (2.4)	33 (2.6)	6 (1.5)
Human Metapneumovirus	42 (2.5)	37 (2.9)	4 (1.0)
Parainfluenza Virus	26 (1.1)	21 (1.6)	5 (1.2)
Coronavirus	13 (0.8)	10 (0.8)	4 (1.0)
Bordetella Pertussis	4 (0.2)	3 (0.2)	1 (0.2)
Mycoplasma Pneumonia	43 (2.6)	37 (2.9)	4 (1.0)
Bokavirus	8 (0.5)	7 (0.5)	0
Streptococcus Pneumoniae	249 (14.8)	176 (14.1)	69 (17.5)
Haemophilus Influenzae	309 (18.4)	232 (18.6)	74 (18.8)
Klebsiella Pneumoniae	48 (2.9)	35 (2.8)	13 (3.3)
Pseudomonas Aeruginosa	163 (9.7)	104 (8.3)	48 (12.2)
Staphylococcus Aureus	110 (6.5)	88 (7.0)	22 (5.5)

Note: This table details the pathogen detection rates in mild and severe cases of acute respiratory infections, including the prevalence of viral and bacterial pathogens

Discussion

This study offers valuable insights into the multifactorial nature of respiratory infection severity, highlighting the significant roles of bacterial co-infections, pre-existing conditions, and clinical symptoms in determining disease outcomes.

Age emerged as a critical determinant of disease severity, with patients aged ≥ 60 years accounting for 28.2% of severe cases. This finding aligns with previous studies demonstrating the increased susceptibility of older adults to severe respiratory infections due to age-related immune decline [5, 6]. However, those aged 0–17 years accounted for a large proportion of mild and severe cases (48.4% of mild cases, 42.5% of severe cases). While this group had a lower risk of severe outcomes, the high proportion of both mild and severe cases underscores the importance of monitoring viral infections in pediatric patients, as they may still contribute significantly to the overall disease burden.

Patients with cardiovascular comorbidities had a significantly higher risk of the development of pneumonia and severe outcomes, aligning with findings showing they are more susceptible to poor outcomes in respiratory infections [7]. The presence of other pre-existing conditions, including endocrine and metabolic disorders, further increases the risk of severe disease. Additionally, pre-existing lung diseases were significantly associated with an increased risk of severe outcomes such as pneumonia (OR = 2.34, 95% CI: 1.48–3.70) and bronchitis (OR = 1.71, 95% CI: 1.03–2.85). Although endocrine diseases (OR = 1.59, 95% CI: 0.87–2.90) and cancer (OR = 1.18, 95% CI: 0.48–2.86) showed elevated odds ratios for severe cases, these associations were not statistically significant, indicating a need for further research with larger sample sizes to clarify their impact on disease severity..

The development of pneumonia was significantly associated with respiratory syncytial virus, influenza A, and influenza B infection. Viral infections, particularly influenza A, were significantly associated with severe cases, corroborating previous studies that underscore the heightened virulence of influenza A during seasonal epidemics and pandemics [8]. Recent studies have further substantiated the association between respiratory syncytial virus infection and an increased risk of pneumonia. For instance, a study published in the International Journal of Infectious Diseases identified several risk factors for respiratory syncytial virus-associated acute lower respiratory tract infections, emphasizing the significant burden of respiratory syncytial virus-related pneumonia, especially among vulnerable populations [9]. Similarly, research has demonstrated that influenza B virus infection is linked to a heightened risk of pneumonia in adults, highlighting the need for vigilant monitoring and management of patients with influenza B to prevent severe respiratory complications [10].

In this study, bacterial pathogens such as *S. pneumoniae* and *P. aeruginosa* were associated with the development of bronchitis. Additionally, *S. pneumoniae* were identified as risk factor that may contribute to severe cases, though it is not possible to confirm from this analysis whether *S. pneumoniae* was involved in co-infection. These findings underscore the necessity of early and accurate detection of both viral and bacterial pathogens, as well as the implementation of targeted therapeutic strategies to mitigate the risk of severe outcomes. Notably, bacterial infections have been identified as a pivotal

Table 3 Distribution of infections and clinical outcomes in acute respiratory infections by pathogen type and Co-Infection status [N (%)]

Indicator	Total	No Infection	Virus Only	Bacteria Only	Co-Infection
Number	1638	343 (20.9)	635 (38.8)	161 (9.8)	499 (30.5)
Age (Years)					
0–17	760	107 (14.1)	253 (33.2)	76 (10.0)	326 (42.9)
18–60	582	142 (24.4)	272 (46.7)	54 (9.3)	114 (19.6)
≥ 60	276	94 (34.1)	106 (38.4)	31 (11.2)	45 (16.3)
Gender					
Male	811	178 (21.9)	287 (35.4)	76 (9.4)	270 (33.3)
Female	827	165 (19.9)	348 (42.1)	85 (10.3)	229 (27.7)
Severity					
Mild	1245	333 (26.8)	423 (33.9)	155 (12.5)	334 (26.8)
Severe	393	10 (2.5)	212 (53.9)	6 (1.5)	165 (42.0)
Complications					
No Complications	1255	301 (24.0)	470 (37.4)	141 (11.2)	343 (27.4)
Bronchitis	169	19 (11.2)	56 (33.1)	13 (7.7)	81 (48.0)
Pneumonia	179	21 (11.7)	99 (55.3)	6 (3.4)	53 (29.6)
Other	49	4 (8.2)	15 (30.6)	2 (4.1)	28 (57.1)
Duration (Days)					
0–6	770	187 (24.3)	311 (40.4)	73 (9.5)	199 (25.8)
7–13	447	76 (17.0)	182 (40.7)	37 (8.3)	152 (34.0)
≥ 14	63	18 (28.6)	21 (33.3)	5 (7.9)	19 (30.2)
Symptoms					
Fever	1217	201 (16.5)	510 (41.9)	93 (7.6)	413 (33.9)
Cough	1267	236 (18.6)	507 (40.0)	119 (9.4)	405 (31.9)
Sputum Production	768	176 (22.9)	312 (40.6)	71 (9.2)	209 (27.2)
Headache	462	92 (19.9)	208 (45.0)	39 (8.4)	129 (27.9)
Fatigue	497	90 (18.1)	226 (45.5)	38 (7.6)	143 (28.8)
Muscle Pain	258	51 (19.7)	134 (51.9)	14 (5.4)	59 (22.9)
Nasal Congestion	320	44 (13.8)	121 (37.8)	26 (8.1)	129 (40.3)
Sore Throat	454	80 (17.6)	195 (42.9)	40 (8.8)	139 (30.6)
Sneezing	210	33 (15.7)	82 (39.0)	1 (0.5)	79 (37.6)
Runny Nose	469	60 (12.8)	178 (38.0)	37 (7.9)	194 (41.4)
Shortness of Breath	56	16 (28.6)	21 (37.5)	4 (7.1)	15 (26.8)
Chest Tightness	71	14 (19.7)	21 (29.6)	8 (11.3)	28 (39.4)
Diarrhea	32	11 (34.4)	11 (34.4)	2 (6.3)	8 (25.0)
Nausea	59	13 (22.0)	27 (45.8)	3 (5.1)	16 (27.1)
Vomiting	71	12 (16.9)	22 (31.0)	4 (5.6)	33 (46.5)
Clinical Outcome					
Cured	716	114 (15.9)	315 (43.9)	62 (8.6)	225 (31.4)
Improved	901	227 (25.2)	318 (35.3)	92 (10.2)	264 (29.3)
Death	2	0 (0.0)	1 (50.0)	1 (50.0)	0 (0.0)

Note: This table illustrated the distribution of pathogens and their associated clinical outcomes in patients with acute respiratory infections

factor in worsening the prognosis of viral respiratory diseases, further emphasizing the need for comprehensive diagnostic and treatment approaches [11, 12].

Moreover, viral-bacterial co-infections were more common in severe cases, particularly with influenza A and *S. pneumoniae*. The positive correlation between Influenza A virus and bacterial infections, such as *S. pneumoniae*, suggests that influenza A may predispose patients to secondary bacterial infections, worsening their clinical outcomes. This aligns with previous studies indicating that viral infections, especially influenza, often facilitate bacterial co-infections by compromising the immune system, leading to more severe disease manifestations [7]. Interestingly, while influenza B and rhinovirus were also associated with bacterial co-infections, their correlation was weaker compared to influenza A, which highlights the distinct severity profiles of different viral pathogens.

The predictive value of clinical symptoms in assessing disease severity was also investigated. Symptoms such as fever, cough, and dyspnea were significantly associated

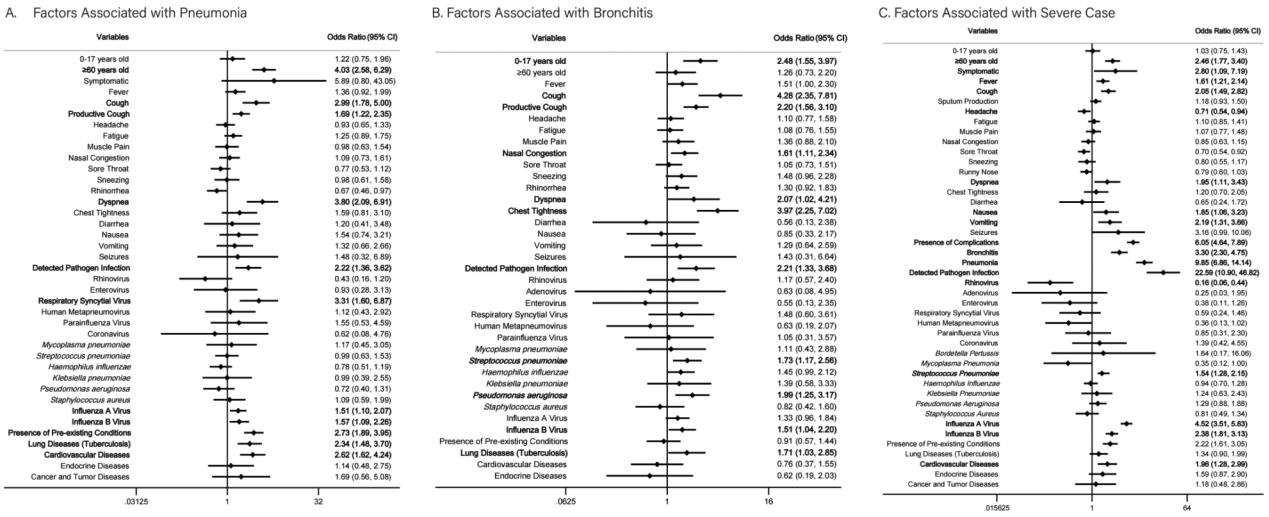

Fig. 1 Factors Associated with Severe Cases of Acute Respiratory Infections. Note: The association between each factor and the disease severity was analyzed by multiple logistic regression adjusted for age group, gender, BMI, residential area, illness onset months, and smoking status; aOR = adjusted Odds Ratio; CI = Confidence Interval

with severe cases, reaffirming their utility as critical indicators for clinicians in identifying high-risk patients. Although less frequently observed, symptoms such as vomiting and nausea were highly indicative of severe disease, necessitating closer monitoring and timely intervention. Additionally, the presence of multi-symptom presentations may serve as a valuable tool for identifying patients at elevated risk of complications, particularly those with co-infections or underlying chronic health conditions. These findings highlight the importance of a comprehensive clinical evaluation to guide early intervention and improve patient outcomes.

This study has several limitations that should be considered when interpreting the results. First, key patient characteristics such as vaccination status and lifestyle factors (e.g., alcohol use and physical activity) were not included in the analysis, and these factors could potentially influence disease outcomes. For example, vaccination status might affect the severity of respiratory infections, with vaccinated individuals generally experiencing milder disease courses. Second, the study relied on data collected from patients in a specific geographic area from September 2023 to April 2024. The period primarily focuses on the autumn and winter months, which are typically associated with higher rates of respiratory infections. However, this time-frame may not fully capture the seasonal variation in respiratory infections, potentially affecting pathogen distribution and disease severity. Additionally, the study's geographic limitation may affect the generalizability of the findings to other regions with different population characteristics or healthcare systems. Third, we could not confirm co-infection in some cases, as the study only identified pathogens based on nucleic acid detection, and bacterial co-infections were not always verified through culture or other confirmatory methods. Furthermore, the study did not verify whether patients had received any medication prior before seeking treatment. For instance, antibiotic used before treatment could alter the pathogen profile or obscure certain infections. Lastly, while the study controlled for several confounding factors, unmeasured variables, such as socioeconomic status and healthcare access, may still influence the severity of respiratory infections and clinical outcomes. Moreover, our study design allows for the identification of associations but does not establish causality. Future longitudinal follow-up studies are warranted to enhance our understanding of disease dynamics. These limitations highlight the need for further research that incorporates a broader range of factors to better understand the complexities of respiratory infection severity.

Conclusions

In conclusion, this study underscores the complex interplay of factors influencing respiratory infection severity, including bacterial co-infections, pre-existing conditions, and clinical symptoms. These findings emphasize the importance of early detection and targeted treatment strategies to improve outcomes in high-risk populations. Key risk factors include the development of pneumonia and bronchitis, co-infection, and pre-existing health conditions such as cardiovascular disease. Age, clinical symptoms, and viral pathogens (particularly influenza A and B) were significantly associated with severe outcomes. These findings underscore the importance of early detection, targeted treatment, and preventative

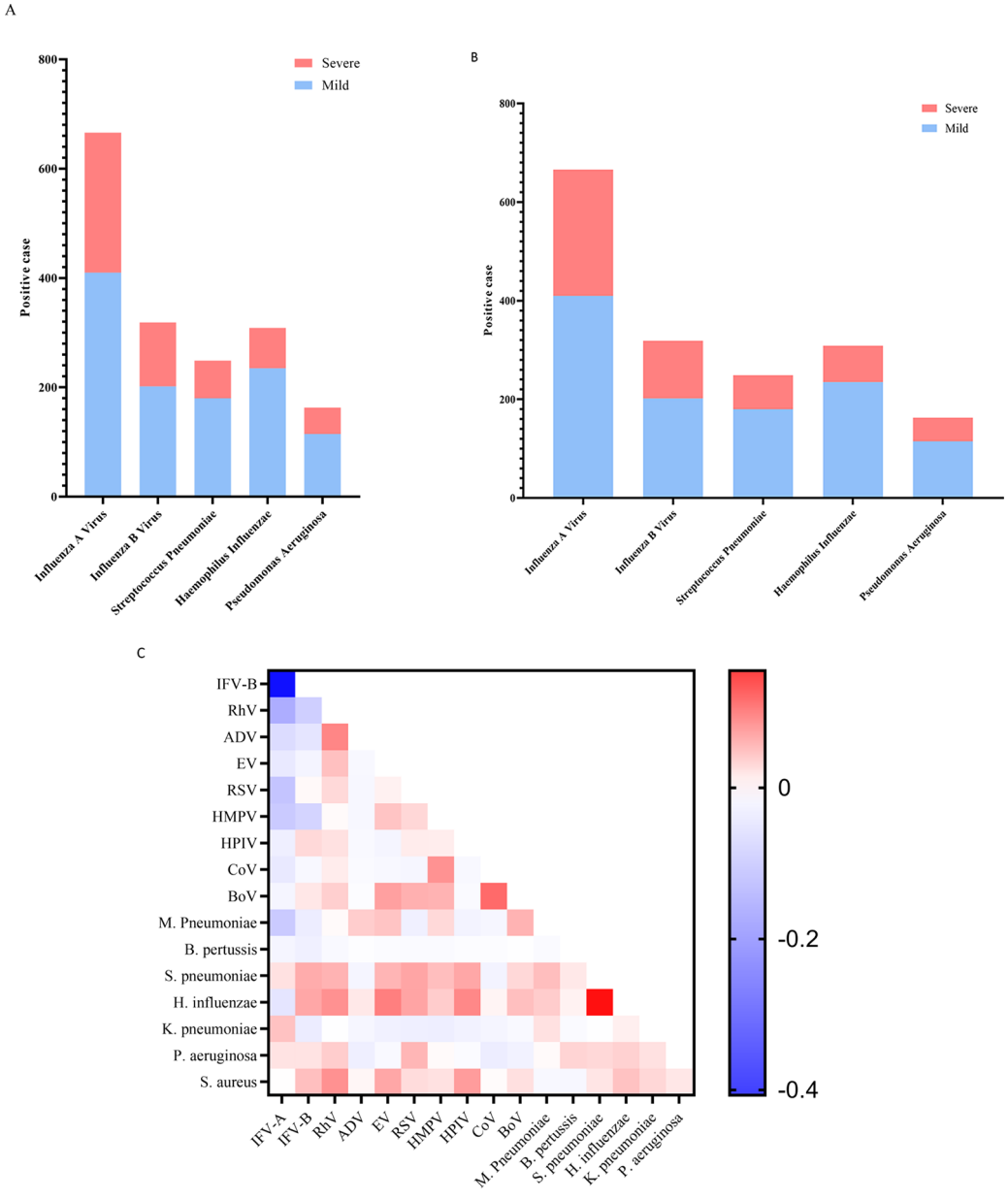

Fig. 2 Clinical Symptoms and Severity in Patients with Acute Respiratory Infections. **A**: Pathogen Detection cases in Severe and Mild Acute Respiratory Infections (1 N_{case}≥100). **B**: Pathogen Detection cases in Severe and Mild Acute Respiratory Infections (N_{case}<100). **C**: Heat map of Pearson correlation coefficients for pathogens pair comparison. Abbreviation: RSV = Respiratory Syncytial Virus; HPIV = Human Parainfluenza Virus; CoV = Coronavirus; BoV = Bocavirus; *M. Pneumoniae* = *Mycoplasma Pneumoniae*; *B. pertussis* = *Bordetella PertussisS. pneumoniae* = *Streptococcus pneumoniae*; *H. influenzae* = *Haemophilus influenzae*; *P. aeruginosa* = *Pseudomonas aeruginos*a; *S. aureus* = *Staphylococcus aureus*

strategies to improve outcomes in patients with respiratory infections, particularly in high-risk populations such as older adults and those with chronic diseases.

Abbreviations

BMI	Body mass index
APACHE II	Acute physiology and chronic health evaluation II
qSOFA	Quick sequential organ failure assessment
PCR	Polymerase chain reaction
qPCR	Quantitative polymerase chain reaction
S. pneumoniae	Streptococcus pneumoniae
H. influenzae	Haemophilus influenzae
K. pneumoniae	Klebsiella pneumoniae
P. aeruginosa	Pseudomonas aeruginosa
S. aureus	Staphylococcus aureus
M. pneumoniae	Mycoplasma pneumoniae
COPD	Chronic obstructive pulmonary disease
CI	Confidence interval
OR	Odds ratio

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12879-025-11121-z.

Supplementary Material 1

Supplementary Material 2

Acknowledgements
Not applicable.

Author contributions
L.F., W.T., and Z.W. supervised and designed the study and revised the manuscript. Y.X., L.Q., Y.D., and J.Y. analyzed the data. Y.X., Y.D., M.J., Y.C., and Y.S. wrote the original draft. All authors read and approved the final manuscript.

Funding
Supported by Science & Technology Fundamental Resources Investigation Program (2023FY100600), the Chinese Academy of Medical Sciences Innovation Fund for Medical Sciences(2022-I2M-CoV19-006), the Beijing Natural Science Foundation (L222028), and the Special Funds for the Basic Research and Development Program in the Central Non-profit Research Institutes of China (2021-RC330-002).

Data availability
Due to the potentially sensitive information included, the original dataset is not public and is available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
The ethical approval of the project was conducted and approved by the Institutional Review Board of the Chongqing Center for Disease Control and Prevention (Identifier: 2023-KY-028-2) in accordance with the principles of the Declaration of Helsinki and Ethical Review Guidelines for Biomedical Research Involving Human Subjects, and informed consent was obtained from all relevant personnel. All questionnaires were reviewed by the attending physicians of the patients to ensure that the information provided was consistent with the data in the Hospital Information System(Additional file 2).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Public Health Emergency Management Innovation Center, State Key Laboratory of Respiratory Health and Multimorbidity, Key Laboratory of Pathogen Infection Prevention and Control (Peking Union Medical College), School of Population Medicine and Public Health, Ministry of Education, Chinese Academy of Medical Science & Peking Union Medical College, Beijing, China
[2]Chongqing Municipal Center for Disease Control and Prevention, Chongqing, China

Received: 13 February 2025 / Accepted: 15 May 2025
Published online: 23 May 2025

References

1. GBD 2021 Causes of Death Collaborators. Global burden of 288 causes of death and life expectancy decomposition in 204 countries and territories and 811 subnational locations, 1990–2021: a systematic analysis for the global burden of disease study 2021. Lancet. 2024;403:2100–32.
2. Zhang L, Wu M. Age-related factors in respiratory infection severity. Clin Microbiol Rev. 2019;32:123–35.
3. Chen Y, Liu X. Impact of Streptococcus pneumoniae and Haemophilus influenzae in severe respiratory infections. Infect Dis J. 2021;50:567–72.
4. Williams K, Smith J, Brown R, Taylor M, Johnson P, Wilson A, et al. Complications in influenza A virus infections. Lancet Infect Dis. 2020;21:1132–41.
5. Adams R, Scott D, Campbell N, Perez L, Nelson W, Hall K, et al. Predictive value of symptoms in respiratory infections. Clin Infect Dis. 2020;59:890–9.
6. Lee D, Kim J, Park S, Choi Y, Lim H, Cho B, et al. Influenza B and severe respiratory disease: a clinical study. J Viral Infect. 2020;48:101–7.
7. Yang F, Liu S. Influenza A and B viruses: epidemiology and clinical outcomes. Viral Dis Rev. 2021;56:443–56.
8. Wang X, Sun H. Bacterial superinfections in influenza patients. J Clin Microbiol. 2021;59:135–44.
9. Smith J, Doe A. Risk factors for RSV-associated pneumonia in children: A systematic review. Int J Infect Dis. 2024;135:45–52.
10. Lee K, Park S. Influenza B virus infection and the risk of pneumonia in adults: A retrospective cohort study. Am J Infect Control. 2023;51(7):789–95.
11. Thomas R, Robinson M. Cardiovascular disease and its role in respiratory infection severity. Heart J. 2021;45:90–101.
12. Miller S, Davis L, Harris B, Clark T, White E, Martinez G, et al. Age and immune system dysfunction in respiratory diseases. J Aging Res. 2019;22:56–64.

Publisher's note