Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Clinical characteristics and risk factors for Influenza A(H1N1) complicated by bacterial pneumonia: a retrospective study

Yiping Li
Xi'an DaXing Hospital
Xiaojuan Yang
Xi'an DaXing Hospital
Yuhang Wan
Xi'an DaXing Hospital
Taotao Li
Xi'an DaXing Hospital
Qing Wei
674003501@qq.com

Xi'an DaXing Hospital

Research Article

Keywords: influenza A(H1N1), bacterial pneumonia, risk factors, hypoproteinemia, chronic respiratory diseases

Posted Date: June 29th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10022593/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License

Additional Declarations: No competing interests reported.

Abstract

Background

Influenza imposes a major global public health burden, and bacterial pneumonia is a serious complication of influenza. However, studies on bacterial pneumonia complicating influenza A(H1N1) have remained limited in recent years. This study aimed to investigate the clinical characteristics and independent risk factors for bacterial pneumonia in hospitalized adult patients with influenza A(H1N1).

Methods

A retrospective analysis was performed in 460 adult patients with influenza A(H1N1) who were admitted to a tertiary general hospital in Xi'an between November 2023 and February 2025. Demographic characteristics, clinical manifestations, laboratory findings, microbiological results, and clinical outcomes were collected. According to the presence or absence of bacterial pneumonia, patients were classified into the bacterial pneumonia group and the non-bacterial pneumonia group. Clinical characteristics were compared between groups. Univariable analysis was used to screen for potential risk factors, and multivariable logistic regression analysis was performed to identify independent risk factors.

Results

Among the 460 patients, 412 were assigned to the non-bacterial pneumonia group and 48 to the bacterial pneumonia group. Patients in the bacterial pneumonia group were older, more frequently male, and had a higher prevalence of chronic respiratory diseases, sputum production, and dyspnea. They also had significantly higher white blood cell and neutrophil counts, as well as higher C-reactive protein and procalcitonin levels. Hypoproteinemia on admission was more common in the bacterial pneumonia group. In addition, the bacterial pneumonia group had higher rates of mechanical ventilation and severe pneumonia, as well as a longer hospital stay ($P < 0.05$). Among the 48 patients in the bacterial pneumonia group, the three most common bacterial isolates from respiratory specimens were *Klebsiella pneumoniae* (18.75%), *Acinetobacter baumannii* (18.75%), and *Pseudomonas aeruginosa* (18.75%). Multivariable logistic regression analysis showed that chronic respiratory diseases and hypoproteinemia were independent risk factors for bacterial pneumonia in patients with influenza A(H1N1).

Conclusion

Influenza A(H1N1) complicated by bacterial pneumonia was associated with a stronger inflammatory response and greater clinical severity. Chronic respiratory diseases and hypoproteinemia were identified as independent risk factors.

Introduction

Influenza poses a substantial threat to public health. Most individuals infected with influenza virus develop only mild respiratory symptoms. However, immunocompromised patients are more likely to progress to severe disease, with a correspondingly increased risk of mortality [1–3]. The 1918 influenza A(H1N1) pandemic caused an estimated 20–50 million deaths worldwide [4], whereas the 2009 influenza A(H1N1) pandemic resulted in approximately 28 million deaths globally [5]. In the post-pandemic era, influenza A(H1N1)pdm09 has become one of the major circulating strains of seasonal influenza [6]. Notably, bacterial pneumonia is among the most serious complications of influenza infection, placing affected patients at increased risk of severe illness and mortality and imposing a substantial burden on both patients and healthcare systems [7, 8].

Patients with influenza complicated by bacterial pneumonia often experience rapid clinical deterioration, and severe coinfection is associated with an increased risk of adverse outcomes across all age groups [9, 10]. However, the mechanisms underlying virus–bacterium interactions remain incompletely understood, and current preventive and therapeutic strategies are still largely limited to antiviral therapy, antibacterial treatment, and vaccination [11]. In addition, population aging and the widespread use of antimicrobial agents have altered pathogen epidemiology and antimicrobial resistance patterns, posing substantial challenges to the timely selection of appropriate empiric antimicrobial therapy [12]. Consequently, the prevention and management of influenza-associated bacterial infection remain major challenges in clinical practice. Early recognition of bacterial infection, risk stratification, and timely targeted intervention are essential for improving clinical outcomes and promoting the rational use of antimicrobial agents. In recent years, clinical data from China on influenza A complicated by bacterial pneumonia have remained limited. Therefore, this study retrospectively analyzed the clinical data of adult inpatients with influenza A(H1N1) complicated by bacterial pneumonia who were admitted to a tertiary care hospital in Xi'an during the 2023–2025 influenza season, with the aim of characterizing their clinical features and identifying associated risk factors, thereby providing evidence to improve clinical recognition and management of this condition.

Methods

Study Population

This retrospective case-control study included adult inpatients with influenza A(H1N1) who were admitted to a tertiary general hospital in Xi'an over three influenza seasons, from November 2023 to February 2025. The hospital is a 2,550-bed tertiary care center with an annual outpatient volume of more than 1.5 million visits. Patients were screened according to the predefined inclusion and exclusion criteria and were then categorized into the bacterial pneumonia group or the non-bacterial pneumonia group based on whether bacterial pneumonia was present.

Inclusion and exclusion criteria

The inclusion criteria were as follows: (1) age ≥ 18 years; (2) hospitalization stay > 24 hours; (3) fulfillment of the diagnostic criteria for influenza A(H1N1); and (4) for patients in the bacterial pneumonia group, fulfillment of the diagnostic criteria for bacterial pneumonia.

The exclusion criteria were as follows: (1) incomplete clinical data; (2) co-infection with other respiratory viruses, including influenza B virus or severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); and (3) concomitant pulmonary fungal infection, pulmonary tuberculosis, or severe bacterial or fungal infections at extrapulmonary sites.

According to the Diagnosis and Treatment Guidelines for Influenza (2025 Edition) [11], influenza A(H1N1) was diagnosed on the basis of a positive influenza virus nucleic acid test together with at least one of the following clinical manifestations: fever, headache, myalgia or generalized body aches, cough, sore throat, rhinorrhea or nasal congestion, systemic symptoms such as chills and fatigue, or less common gastrointestinal symptoms including vomiting or diarrhea.

The diagnosis of bacterial pneumonia was based on relevant clinical guidelines for community-acquired pneumonia and hospital-acquired pneumonia [13, 14] and required the presence of the following: (1) recurrent or persistent high fever, worsening cough, purulent sputum production, or dyspnea; (2) pulmonary infiltrates or consolidation on chest imaging; (3) an elevated peripheral white blood cell count (WBC), an increased neutrophil (NEU) proportion, or markedly elevated procalcitonin (PCT) or C-reactive protein (CRP) levels; and (4) a positive bacterial culture from respiratory specimens, including qualified sputum, bronchoalveolar lavage fluid, or pleural fluid.

Data collection

Clinical data were extracted from the hospital's electronic medical record system, including demographic characteristics (age, sex, smoking history, and underlying comorbidities), clinical manifestations, laboratory test results, bacterial culture and antimicrobial susceptibility results, treatment, and prognosis.

Statistical analysis

All statistical analyses were performed using R software, version 4.1.0. Continuous variables were expressed as the median and interquartile range (IQR) and compared between the bacterial pneumonia group and the non-bacterial pneumonia group using the Mann–Whitney U test. Categorical variables were presented as number (percentage) and compared using the χ^2 test or Fisher's exact test, as appropriate. Logistic regression analysis was performed to identify risk factors for bacterial pneumonia in patients with influenza A(H1N1). A two-sided *P* value < 0.05 was considered statistically significant.

Results

General characteristics

Between November 2023 and February 2025, a total of 610 adult patients were diagnosed with influenza A(H1N1). Of these, 460 met the inclusion and exclusion criteria, including 48 patients (10.4%) in the bacterial pneumonia group and 412 patients (89.6%) in the non-bacterial pneumonia group. The median age of patients in the bacterial pneumonia group was 69.5 (65.0, 78.5) years, which was significantly higher than that in the non-bacterial pneumonia group (65.0 [55.0, 75.0] years; P = 0.012). The proportion of male patients was also higher in the bacterial pneumonia group than in the non-bacterial pneumonia group (72.92% [35/48] vs. 53.88% [222/412], P = 0.012). The prevalence of chronic respiratory diseases (CRDs) was significantly higher in the bacterial pneumonia group than in the non-bacterial pneumonia group (41.67% [20/48] vs. 25.00% [103/412], P = 0.014). No statistically significant differences were observed between the two groups with respect to smoking status, the presence of underlying diseases, or the distribution of other comorbidities, including hypertension, diabetes mellitus, chronic heart disease, and cerebrovascular disease (all P > 0.05), as shown in Table 1.

Table 1
Characteristics of hospitalized adult patients with influenza A(H1N1) included in this study

Variables	non-bacterial pneumonia group (n = 412)	bacterial pneumonia group (n = 48)	P value
Age [a, years]	65 (55, 75)	69.5 (65, 78.5)	0.012
Body temperature [a, °C]	38.3 (37.3, 38.8)	38.3 (36.9, 38.9)	0.685
WBC [a×10^9/L]	5.96 (4.59, 7.51)	9.04 (5.48, 10.81)	< 0.001
NEU [a×10^9/L]	4.26 (3.02, 5.82)	6.83 (3.7, 8.99)	< 0.001
LYM [a×10^9/L]	0.85 (0.57, 1.26)	0.86 (0.44, 1.39)	0.720
PLT [a×10^9/L]	175.0 (137.0, 220.0)	159.5 (116.5, 222.0)	0.249
HGB [a, g/L]	127.0 (116.0, 141.0)	128.0 (107.5, 144.5)	0.729
CRP [a, mg/L]	16.25 (7.27,41.18)	44.54 (21.90, 108.41)	< 0.001
PCT [a, ng/mL]	0.08 (0.04, 0.17)	0.31 (0.07, 2.08)	< 0.001
Hypoproteinemia, n (%)			< 0.001
No	335 (81.31)	26 (54.17)	
Yes	77 (18.69)	22 (45.83)	
Sex, n (%)			0.012
Male	222 (53.88)	35 (72.92)	
Female	190 (46.12)	13 (27.08)	
Smoking status, n (%)			0.882
No	313 (75.97)	36 (75.00)	
Yes	99 (24.03)	12 (25.00)	
Underlying diseases, n (%)			0.288
None	57 (13.83)	4 (8.33)	
Present	355 (86.17)	44 (91.67)	
Hypertension, n (%)			0.715
No	226 (54.85)	25 (52.08)	
Yes	186 (45.15)	23 (47.92)	
Hyperlipidemia, n (%)			0.129
No	393 (95.39)	48 (100.00)	
Yes	19 (4.61)	0 (0.00)	
Diabetes, n (%)			0.389
No	299 (72.57)	32 (66.67)	
Yes	113 (27.43)	16 (33.33)	
CRDs, n (%)			0.014
No	309 (75.00)	28 (58.33)	
Yes	103 (25.00)	20 (41.67)	
Chronic heart disease, n (%)			0.323
No	270 (65.53)	28 (58.33)	

[a] M(P_{25}-P_{75}) nterquartile range; n (%), number (percent); WBC, white blood cell; NEU, neutrophil; LYM, lymphocyte; PLT, platelet; HGB, hemoglobin; CRP, C-reactive protein; PCT, procalcitonin; CRDs, Chronic respiratory diseases; LOS, length of hospital stay

Variables	non-bacterial pneumonia group (n = 412)	bacterial pneumonia group (n = 48)	P value
Yes	142 (34.47)	20 (41.67)	
Chronic kidney disease, n (%)			0.453
No	383 (92.96)	46 (95.83)	
Yes	29 (7.04)	2 (4.17)	
Chronic liver disease, n (%)			0.553
No	364 (88.35)	41 (85.42)	
Yes	48 (11.65)	7 (14.58)	
Hematological disorders, n (%)			1.000
No	390 (94.66)	45 (93.75)	
Yes	22 (5.34)	3 (6.25)	
Cerebrovascular disease, n (%)			0.471
No	287 (69.66)	31 (64.58)	
Yes	125 (30.34)	17 (35.42)	
Malignant tumors, n (%)			0.483
No	366 (88.83)	41 (85.42)	
Yes	46 (11.17)	7 (14.58)	
Cough, n (%)			0.486
No	77 (18.69)	7 (14.58)	
Yes	335 (81.31)	41 (85.42)	
Sputum production, n (%)			0.047
No	135 (32.77)	9 (18.75)	
Yes	277 (67.23)	39 (81.25)	
Dyspnea, n (%)			0.013
No	280 (67.96)	24 (50.00)	
Yes	132 (32.04)	24 (50.00)	
Gastrointestinal symptoms, n (%)			1.000
No	381 (92.48)	44 (93.44)	
Yes	31 (7.52)	4 (6.56)	
Fatigue, n (%)			0.229
No	341 (82.77)	43 (89.58)	
Yes	71 (17.23)	5 (10.42)	
Muscle pain, n (%)			0.328
No	347 (84.22)	43(89.58)	
Yes	65 (15.78)	5 (10.42)	
Sore throat, n (%)			0.198
No	360 (87.38)	45 (93.75)	
Yes	52 (12.62)	3 (6.25)	
Dizziness or headache, n (%)			0.435

[a] M(P_{25}-P_{75}) nterquartile range; n (%), number (percent); WBC, white blood cell; NEU, neutrophil; LYM, lymphocyte; PLT, platelet; HGB, hemoglobin; CRP, C-reactive protein; PCT, procalcitonin; CRDs, Chronic respiratory diseases; LOS, length of hospital stay

Variables	non-bacterial pneumonia group (n = 412)	bacterial pneumonia group (n = 48)	P value
No	352 (85.44)	43 (89.58)	
Yes	60 (14.56)	5 (10.42)	
Mechanical ventilation, n (%)			< 0.001
No	409 (92.48)	34 (70.83)	
Yes	3 (7.52)	14 (29.17)	
Severe pneumonia, n (%)			< 0.001
No	408 (99.03)	35 (72.92)	
Yes	4 (0.97)	13 (27.08)	
LOS [[a], days]	9 (6, 11)	12 (9, 17)	< 0.001

[a] M(P_{25}-P_{75}) nterquartile range; n (%), number (percent); WBC, white blood cell; NEU, neutrophil; LYM, lymphocyte; PLT, platelet; HGB, hemoglobin; CRP, C-reactive protein; PCT, procalcitonin; CRDs, Chronic respiratory diseases; LOS, length of hospital stay

Clinical symptoms

There were significant between-group differences in the proportions of patients presenting with sputum production and dyspnea (both P < 0.05). Specifically, sputum production was more common in the bacterial pneumonia group than in the non-bacterial pneumonia group (81.25% [39/48] vs. 67.23% [277/412], P = 0.0047). Similarly, dyspnea was more frequent in the bacterial pneumonia group than in the non-bacterial pneumonia group (50.00% [24/48] vs. 32.04% [132/412], P = 0.013). No significant between-group differences were observed in the proportions of patients with cough, gastrointestinal symptoms, fatigue, myalgia, throat discomfort, dizziness, or headache (all P > 0.05), as shown in Table 1.

Laboratory findings

Compared with the non-bacterial pneumonia group, the bacterial pneumonia group had significantly higher WBC, NEU, CRP, PCT levels, and a higher proportion of hypoproteinemia (all P < 0.001). Specifically, the median WBC was 5.96 (4.59, 7.51) × 10^9/L in the non-bacterial pneumonia group and 9.04 (5.48, 10.81) × 10^9/L in the bacterial pneumonia group (P < 0.001). The median NEU was 4.26 (3.02, 5.82) × 10^9/L in the non-bacterial pneumonia group and 6.83 (3.74, 8.99) × 10^9/L in the bacterial pneumonia group (P < 0.001). The median CRP level was 16.25 (7.27, 41.18) mg/L in the non-bacterial pneumonia group and 44.54 (21.90, 108.41) mg/L in the bacterial pneumonia group (P < 0.001). The median PCT level was 0.08 (0.04, 0.17) ng/mL in the non-bacterial pneumonia group and 0.31 (0.07, 2.08) ng/mL in the bacterial pneumonia group (P < 0.001). In addition, hypoproteinemia (serum albumin < 35 g/L) was more common in the bacterial pneumonia group than in the non-bacterial pneumonia group (45.83% vs. 18.69%, P < 0.001). No significant between-group differences were observed in lymphocyte count (LYM), platelet count (PLT), or hemoglobin (HGB) level (all P > 0.05). Detailed results are presented in Table 1.

Microbiological culture and antimicrobial susceptibility results

The bacterial pneumonia group comprised 48 patients. A total of 53 culture-positive specimens of acceptable quality were collected, yielding 48 non-duplicate bacterial isolates. Specimen types included 33 sputum samples, 18 bronchoalveolar lavage Fluid (BALF) samples, and 2 blood samples. Among these patients, 5 had positive cultures from multiple specimen types simultaneously: 3 had both sputum and BALF cultures positive, 1 had both sputum and blood cultures positive, and 1 had both BALF and blood cultures positive. In this study, when the same pathogen was isolated from different specimens obtained from the same patient, it was counted as a single isolate and was not included repeatedly in the analysis.

The isolated pathogens included 9 strains of *Klebsiella pneumoniae* (*K. pneumoniae*) (18.75%), 9 strains of *Acinetobacter baumannii* (*A. baumannii*) (18.75%), 9 strains of *Pseudomonas aeruginosa* (*P. aeruginosa*) (18.75%), 7 strains of *Haemophilus influenzae* (*H. influenzae*) (14.58%), 4 strains of *Streptococcus pneumoniae* (*S. pneumoniae*) (8.34%), 4 strains strains of *Staphylococcus aureus* (*S. aureus*) (8.34%), 3 strains of *Moraxella catarrhalis* (*M. catarrhalis*) (6.25%), 1 strain of *Enterobacter hormaechei* (*E. hormaechei*) (2.08%), 1 strains of *Escherichia coli* (*E. coli*) (2.08%), and 1 strains of *Serratia marcescens* (*S. marcescens*) (2.08%), as shown in Table 2.

The antimicrobial susceptibility profiles of Gram-negative isolates are shown in Table 3, and the antimicrobial susceptibility profiles of Gram-positive isolates are shown in Table 4. Among the *A. baumannii* isolates, 7 were identified as carbapenem-resistant *A. baumannii* (CRAB). In addition, 2 *S. aureus* isolates were identified as methicillin-resistant *S. aureus* (MRSA), and both were susceptible to vancomycin.

Table 2
Distribution of bacterial isolates in the bacterial pneumonia group

Pathogen Group	Species	No. of Isolates	Proportion (%)
GNB	*K. pneumoniae*	9	18.75
	A. baumannii	9	18.75
	P. aeruginosa	9	18.75
	H. influenzae	7	14.58
	M. catarrhalis	3	6.25
	E. hormaechei	1	2.08
	E. coli	1	2.08
	S. marcescens	1	2.08
GPB	*S. aureus*	4	8.34
	S. pneumoniae	4	8.34
Total		48	100.00
GNB, Gram-negative bacteria; GPB, Gram-positive bacteria			

Table 3
Antimicrobial resistance profiles of Gram-negative isolates

Antibiotic agent	*K. pneumoniae* (n = 9)	*A. baumannii* (n = 9)	*P. aeruginosa* (n = 9)	*H. influenzae* (n = 7)	*M. catarrhalis* (n = 3)	*E. hormaechei* (n = 1)	*E. coli* (n = 1)	*S. marcescens* (n = 1)
ampicillin/sulbactam	1 (11.1)	7 (77.8)	NA	3 (42.9)	NA	1 (100.0)	0 (0.0)	0 (0.0)
cefazolin	1 (11.1)	NA	NA	NA	NA	1 (100.0)	1 (100.0)	0 (0.0)
ceftriaxone	1 (11.1)	7 (77.8)	NA	0	NA	1 (100.0)	1 (100.0)	0 (0.0)
piperacillin/tazobactam	0 (0.0)	7 (77.8)	2 (22.2)	NA	NA	1 (100.0)	0 (0.0)	0 (0.0)
meropenem	0 (0.0)	7 (77.8)	0	0	NA	0 (0.0)	0 (0.0)	0 (0.0)
imipenem	0 (0.0)	7 (77.8)	0	NA	NA	0 (0.0)	0 (0.0)	0 (0.0)
ciprofloxacin	1 (11.1)	8 (88.9)	2 (22.2)	NA	NA	0 (0.0)	0 (0.0)	0 (0.0)
tobramycin	0 (0.0)	7 (77.8)	NA	NA	NA	0 (0.0)	0 (0.0)	1 (100.0)
trimethoprim/sulfamethoxazole	1 (11.1)	7 (77.8)	NA	5 (71.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Data are presented as n (%). NA, not available/not tested

Table 4
Antimicrobial resistance profiles of Gram-positive isolates

Antibiotic agent	*S. pneumoniae* (n = 4)	*S. aureus* (n = 4)
penicillin	0 (0.0)	4 (100.0)
oxacillin	NA	2 (50.0)
ceftriaxone	0 (0.0)	NA
vancomycin	0 (0.0)	0 (0.0)
linezolid	0 (0.0)	0 (0.0)

Data are presented as n (%). NA, not available/not tested

Treatment and clinical outcomes

Patients in both the bacterial pneumonia group and the non-bacterial pneumonia group received standard antiviral therapy for 5 days after testing positive for influenza A(H1N1) virus, although the duration of antiviral treatment was extended to 10 days in some critically ill patients. Significant differences were observed between the two groups in the incidence of severe pneumonia and length of hospital stay (both $P < 0.05$). The rate of mechanical ventilation was significantly higher in the bacterial pneumonia group than in the non-bacterial pneumonia group (29.17% [14/48] vs. 7.52% [3/412], P < 0.001). In addition, the length of hospital stay was significantly longer in the bacterial pneumonia group than in the non-bacterial pneumonia group (12.0 [9.0, 17.0] days vs. 9.0 [6.0, 11.0] days, P < 0.001). The incidence of severe pneumonia was also significantly higher in the bacterial pneumonia group than in the non-bacterial pneumonia group (27.08% [13/48] vs. 0.97% [4/412], P < 0.001), as shown in Table 1.

Multivariable logistic regression analyses

Univariable analysis identified age, sex, CRDs, hypoalbuminemia, and length of hospital stay as factors associated with bacterial pneumonia in patients with influenza A(H1N1) (P < 0.05). Variables that were statistically significant in the univariable analysis were subsequently included in the multivariable logistic regression model. After adjustment for potential confounders, length of hospital stay (P = 0.047), CRDs (P = 0.029), and hypoalbuminemia (P = 0.001) remained independently associated with bacterial pneumonia in patients with influenza A(H1N1). Among these, CRDs and hypoalbuminemia were identified as independent risk factors, whereas the association between length of hospital stay and bacterial pneumonia (OR = 0.963, 95% CI 0.929–1.000) should be interpreted with caution in the clinical context, as shown in Table 5.

Table 5
Logistic regression analysis of factors for bacterial pneumonia complicating influenza A(H1N1)

Predictor	β	SE	Wald	OR	95% CI	P value
Age	-0.016	0.012	1.641	0.984	0.961–1.008	0.2
Male sex	-0.623	0.355	3.077	0.537	0.268–1.076	0.079
CRDs	0.741	0.34	4.753	2.098	1.078–4.083	0.029
Hypoproteinemia	1.175	0.338	12.09	3.238	1.670–6.278	0.001
Length of hospital stay	-0.037	0.019	3.941	0.963	0.929-1.000	0.047

OR, odds ratio; CI, confidence interval; SE, standard error; CRDs, chronic respiratory diseases

Discussion

The present study showed that the incidence of bacterial pneumonia among patients with influenza A(H1N1) was 7.87% (48/610). MacIntyre et al. [15] reported that during the 2009 influenza A(H1N1) pandemic, the mean rate of bacterial coinfection among hospitalized patients was 19%. A meta-analysis [16] found that the prevalence of bacterial coinfection in patients with influenza ranged from 2% to 65%, with substantial heterogeneity across studies ($I^2 = 95\%$). The incidence observed in our study falls within this reported range. The clinical manifestations of influenza A(H1N1) complicated by bacterial pneumonia are nonspecific. In the present study, patients in the bacterial pneumonia group were more likely to present with productive cough and dyspnea, suggesting increased airway secretions and impaired ventilatory function. In addition, the incidences of respiratory failure and severe pneumonia were significantly higher in the bacterial pneumonia group than in the non-bacterial pneumonia group, further supporting the association between bacterial pneumonia and worse clinical outcomes [17]. Clinically, continued deterioration despite 5 days of antiviral therapy should raise suspicion for concomitant bacterial infection. Laboratory findings further showed that PCT and CRP levels were significantly higher in the bacterial pneumonia group, which is consistent with the findings of Li et al. [18]. Ingram et al. [19] also reported that in patients with 2009 influenza A(H1N1), elevated PCT levels were often associated with poor prognosis, whereas low PCT and CRP levels suggested a lower likelihood of bacterial infection. Collectively, these findings suggest that combined assessment of PCT and CRP may be valuable for the early identification of bacterial coinfection in patients with influenza A.

Among the 48 patients in the bacterial pneumonia group, 41 developed community-acquired pneumonia (CAP), whereas 7 developed hospital-acquired pneumonia (HAP). During the 2009 influenza A(H1N1) pandemic, *Streptococcus pneumoniae* and *Staphylococcus aureus* were the predominant bacterial pathogens [5]. Previous studies [20, 21] have shown that influenza-associated community-acquired bacterial infections are mainly caused by Gram-positive organisms, particularly *Streptococcus pneumoniae*, whereas Gram-negative organisms are detected more frequently in older adults and in patients with chronic comorbidities; common pathogens include *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* [22, 23]. In the present study, Gram-negative organisms accounted for a relatively high proportion of pathogens among patients with influenza A(H1N1) complicated by CAP, which may be attributable to the high proportion of older patients in this subgroup. This finding is consistent with community-acquired pneumonia guidelines [13], which indicate that older adults are at increased risk of Gram-negative bacterial infection. In all cases of HAP secondary to influenza A(H1N1) in this study, the causative pathogen was CRAB, and all affected patients had undergone mechanical ventilation. Influenza virus infection together with endotracheal intubation may disrupt the airway barrier, impair host immune defenses, and compromise bacterial clearance, thereby predisposing patients to HAP caused by multidrug-resistant Gram-negative organisms [24–26]. The overall resistance profile of Gram-negative isolates in our study was similar to that reported previously [22]. Both MRSA

isolates were susceptible to vancomycin. These microbiological characteristics may be related to prior hospitalization and previous antimicrobial exposure. Therefore, empiric antimicrobial therapy should be selected on the basis of local epidemiology and individual patient-level risk factors.

Multivariable logistic regression analysis in the present study identified hypoalbuminemia and chronic obstructive pulmonary disease (COPD) as independent risk factors for bacterial pneumonia in patients with influenza A(H1N1). Albumin plays important roles in immune regulation, antioxidant defense, and endothelial protection. Reduced serum albumin levels have been associated with both the occurrence and severity of infectious diseases and may serve not only as a warning marker but also as a contributing factor [27]. Wi et al. [28] reported that serum albumin levels at hospital admission predict the need for respiratory or vasopressor support in adults with influenza A(H1N1). Washio et al. [29] further showed that hypoalbuminemia (< 3.5 g/dL) is an independent risk factor for CAP in older adults. Although our findings require further confirmation in prospective studies, early monitoring of albumin levels during hospitalization, risk stratification, and timely nutritional support may help improve clinical outcomes. CRDs, including COPD and chronic bronchitis, are generally associated with poor outcomes in patients with influenza [1, 2]. In such patients, airway epithelial integrity is often compromised and mucociliary clearance is impaired; influenza infection may further damage the airway barrier and facilitate bacterial colonization, ultimately increasing the risk of secondary pulmonary infection [30]. A study from Japan demonstrated that asthma and chronic bronchitis/emphysema are important risk factors for bacterial pneumonia complicating influenza [31], which is consistent with our findings. From a clinical perspective, enhanced airway management and close monitoring of inflammatory status are warranted in these patients to reduce the risk of infectious deterioration and progression to severe disease.

Univariable analysis showed significant differences between the bacterial pneumonia group and the non-bacterial pneumonia group with respect to age, sex, and length of hospital stay; however, none of these variables remained independently associated with bacterial pneumonia complicating influenza A in the multivariable analysis. Older adults are more likely to experience immunosenescence [32], whereas male patients often have a higher burden of underlying comorbidities [33]. Both factors may indirectly increase susceptibility to bacterial infection through impaired immune function and compromised airway defense mechanisms. Prolonged hospitalization is also a common feature associated with poorer clinical outcomes in this population and is itself a recognized risk factor for HAP [34]. Owing to the limitations of the study design, this relationship was not examined in depth in the present study and warrants further investigation in future well-designed studies.

This study has several limitations. First, the sample size was relatively small, and the single-center retrospective design may have introduced selection bias. Second, several potentially relevant variables, including vaccination history, the classes of antimicrobial agents administered, and treatment duration, were not included in the analysis. In addition, immune status was not systematically evaluated, and follow-up data on survival outcomes were unavailable. Finally, this study did not differentiate between influenza A complicated by CAP and influenza A complicated by HAP, although the risk factors for these two conditions may differ. Therefore, multicenter prospective studies with larger sample sizes are needed to further validate the identified risk factors and to develop robust predictive models.

Conclusion

Patients with influenza A(H1N1) complicated by bacterial pneumonia were characterized by older age, male sex, a heightened inflammatory response, productive cough, dyspnea, hypoproteinemia, severe pneumonia, and respiratory failure. CRDs and hypoproteinemia were identified as independent risk factors for bacterial pneumonia complicating influenza A(H1N1). In clinical practice, early identification of high-risk patients, dynamic monitoring of inflammatory and nutritional parameters, prompt correction of hypoproteinemia, and optimized management of underlying respiratory disease may help reduce the risk of secondary bacterial infection and improve patient outcomes.

Declarations

Acknowledgements

We would like to thank all the participants for their contributions to this study.

Author contributions

WQ, YXJ and LYP were involved in study design. WYH and LTT collected clinical data and conducted an analysis, LYP and WQ written the article. All authors read and approved the final version of the manuscript.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Availability of data and materials

All data generated during this study are included in this published article.

Ethics approval and consent to participate

The study was conducted in accordance with the principles of the Declaration of Helsinki. The study was approved by the Ethics Committee of Xi'an Daxing Hospital (No. KY-2026002). In this retrospective study, patients' written informed consent was waived, which was approved by the Ethics Committee of Xi'an Daxing Hospital (No. KY-2026002).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]Department of Pharmacy, Xi'an Daxing Hospital, Xi'an 710003, Shanxi, China

References

1. Arranz-Herrero J, Presa J, Rius-Rocabert S, Utrero-Rico A, Arranz-Arija J, Lalueza A, Escribese MM, Ochando J, Soriano V, Nistal-Villan E. Determinants of poor clinical outcome in patients with influenza pneumonia: A systematic review and meta-analysis. Int J Infect Dis. 2023;131:173–9.
2. Giacchetta I, Primieri C, Cavalieri R, Domnich A, de Waure C. The burden of seasonal influenza in Italy: A systematic review of influenza-related complications, hospitalizations, and mortality. Influenza Other Respir Viruses. 2022;16(2):351–65.
3. Qiao M, Moyes G, Zhu F, Li Y, Wang X. The prevalence of influenza bacterial co-infection and its role in disease severity: A systematic review and meta-analysis. J Glob Health. 2023;13:04063.
4. van der Sluijs KF, van der Poll T, Lutter R, Juffermans NP, Schultz MJ. Bench-to-bedside review: bacterial pneumonia with influenza - pathogenesis and clinical implications. Crit Care. 2010;14(2):219.
5. Metersky ML, Masterton RG, Lode H, File TM Jr., Babinchak T. Epidemiology, microbiology, and treatment considerations for bacterial pneumonia complicating influenza. Int J Infect Dis. 2012;16(5):e321–331.
6. Xie Y, Lin S, Zeng X, Tang J, Cheng Y, Huang W, Li J, Wang D. Two Peaks of Seasonal Influenza Epidemics - China, 2023. China CDC Wkly. 2024;6(36):905–10.
7. Jia L, Xie J, Zhao J, Cao D, Liang Y, Hou X, Wang L, Li Z. Mechanisms of Severe Mortality-Associated Bacterial Co-infections Following Influenza Virus Infection. Front Cell Infect Microbiol. 2017;7:338.
8. Teng F, Liu X, Guo SB, Li Z, Ji WQ, Zhang F, Zhu XM. Community-acquired bacterial co-infection predicts severity and mortality in influenza-associated pneumonia admitted patients. J Infect Chemother. 2019;25(2):129–36.
9. Acus K, Meigher S, Saggar VA, Critically Ill Influenza. A-Positive Patient With Spontaneous Pneumomediastinum, Superimposed Bacterial Pneumonia, and Bilateral Pneumothoraces. Cureus. 2024;16(4):e57778.
10. Khouri A, Helou M, Haj Hussein A, Tanios A, Nakhle R. Acute Respiratory Distress Syndrome Secondary to Influenza A Infection in a Patient With No Significant Risk Factors: A Case Report. Cureus. 2025;17(7):e87803.
11. Chen Y, Li H, Mu J, Peng Y, D'Ursi P, Chen K, Zheng Y. PostInfluenza bacterial infections: Epidemiology, mechanistic insights and emerging treatment approaches. J Infect Public Health. 2026;19(4):103178.
12. Rich HE, McCourt CC, Zheng WQ, McHugh KJ, Robinson KM, Wang J, Alcorn JF. Interferon Lambda Inhibits Bacterial Uptake during Influenza Superinfection. Infect Immun. 2019;87(5).
13. Jones BE, Ramirez JA, Oren E, Soni NJ, Sullivan LR, Restrepo MI, Musher DM, Erstad BL, Pickens C, Vaughn VM, et al. Diagnosis and Management of Community-acquired Pneumonia: An Official American Thoracic Society Clinical Practice Guideline. Am J Respir Crit Care Med. 2026;212(1):24–44.
14. Kalil AC, Metersky ML, Klompas M, Muscedere J, Sweeney DA, Palmer LB, Napolitano LM, O'Grady NP, Bartlett JG, Carratalà J, et al. Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis. 2016;63(5):e61–111.
15. MacIntyre CR, Chughtai AA, Barnes M, Ridda I, Seale H, Toms R, Heywood A. The role of pneumonia and secondary bacterial infection in fatal and serious outcomes of pandemic influenza a(H1N1)pdm09. BMC Infect Dis. 2018;18(1):637.
16. Klein EY, Monteforte B, Gupta A, Jiang W, May L, Hsieh YH, Dugas A. The frequency of influenza and bacterial coinfection: a systematic review and meta-analysis. Influenza Other Respir Viruses. 2016;10(5):394–403.
17. Teng F, Liu X, Guo S-B, Li Z, Ji W-Q, Zhang F, Zhu X-M. Community-acquired bacterial co-infection predicts severity and mortality in influenza-associated pneumonia admitted patients. J Infect Chemother. 2019;25(2):129–36.

18. Song JY, Cheong HJ, Heo JY, Noh JY, Yong HS, Kim YK, Kang EY, Choi WS, Jo YM, Kim WJ. Clinical, laboratory and radiologic characteristics of 2009 pandemic influenza A/H1N1 pneumonia: primary influenza pneumonia versus concomitant/secondary bacterial pneumonia. Influenza Other Respir Viruses. 2011;5(6):e535–43.
19. Ingram PR, Inglis T, Moxon D, Speers D. Procalcitonin and C-reactive protein in severe 2009 H1N1 influenza infection. Intensive Care Med. 2010;36(3):528–32.
20. Bartley PS, Deshpande A, Yu PC, Klompas M, Haessler SD, Imrey PB, Zilberberg MD, Rothberg MB. Bacterial coinfection in influenza pneumonia: Rates, pathogens, and outcomes. Infect Control Hosp Epidemiol. 2022;43(2):212–7.
21. Morris DE, Cleary DW, Clarke SC. Secondary Bacterial Infections Associated with Influenza Pandemics. Front Microbiol. 2017;8:1041.
22. Yi G, de Kraker MEA, Buetti N, Zhong X, Li J, Yuan Z, Zhu W, Zhou J, Zhou H. Risk factors for in-hospital mortality and secondary bacterial pneumonia among hospitalized adult patients with community-acquired influenza: a large retrospective cohort study. Antimicrob Resist Infect Control. 2023;12(1):25.
23. Jorda A, Gabler C, Blaschke A, Wölfl-Duchek M, Gelbenegger G, Nussbaumer-Pröll A, Radtke C, Zeitlinger M, Bergmann F. Community-acquired and hospital-acquired bacterial co-infections in patients hospitalized with Covid-19 or influenza: a retrospective cohort study. Infection. 2024;52(1):105–15.
24. Oliva J, Terrier O. Viral and Bacterial Co-Infections in the Lungs: Dangerous Liaisons. Viruses. 2021;13(9).
25. Rowe HM, Meliopoulos VA, Iverson A, Bomme P, Schultz-Cherry S, Rosch JW. Direct interactions with influenza promote bacterial adherence during respiratory infections. Nat Microbiol. 2019;4(8):1328–36.
26. Kalil AC, Thomas PG. Influenza virus-related critical illness: pathophysiology and epidemiology. Crit Care. 2019;23(1):258.
27. Wiedermann CJ. Hypoalbuminemia as Surrogate and Culprit of Infections. Int J Mol Sci 2021;22(9).
28. Wi YM, Kim JM, Peck KR. Serum albumin level as a predictor of intensive respiratory or vasopressor support in influenza A (H1N1) virus infection. Int J Clin Pract. 2014;68(2):222–9.
29. Washio M, Kondo K, Fujisawa N, Harada E, Tashiro H, Mizokami T, Nogami H, Iwanaga T, Nakanishi Y, Suzuki K, et al. Hypoalbuminemia, influenza vaccination and other factors related to the development of pneumonia acquired outside hospitals in southern Japan: A case-control study. Geriatr Gerontol Int. 2016;16(2):223–9.
30. McCullers JA. The co-pathogenesis of influenza viruses with bacteria in the lung. Nat Rev Microbiol. 2014;12(4):252–62.
31. Shirata M, Ito I, Jo T, Iwao T, Oi I, Hamao N, Nishioka K, Yamana H, Nagase T, Yasunaga H, et al. Factors Associated With the Development of Bacterial Pneumonia Related to Seasonal Influenza Virus Infection: A Study Using a Large-scale Health Insurance Claim Database. Open Forum Infect Dis. 2023;10(5):ofad222.
32. Linehan E, Fitzgerald DC. Ageing and the immune system: focus on macrophages. Eur J Microbiol Immunol (Bp). 2015;5(1):14–24.
33. Zou Q, Zheng S, Wang X, Liu S, Bao J, Yu F, Wu W, Wang X, Shen B, Zhou T, et al. Influenza A-associated severe pneumonia in hospitalized patients: Risk factors and NAI treatments. Int J Infect Dis. 2020;92:208–13.
34. Yakoub M, Elkhwsky F, El Tayar A, El Sayed I. Hospital-acquired pneumonia pattern in the intensive care units of a governmental hospital: A prospective longitudinal study. Ann Afr Med. 2023;22(1):94–100.