Predictors of Severe Influenza Community-Acquired Pneumonia in A Multicentre Singapore Cohort of Hospitalised Adults

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KEY MESSAGE

In a multicentre Singapore cohort of adults hospitalised with community-acquired influenza pneumonia (CAP), severe illness was more strongly associated with early physiological derangement at presentation, as measured by the National Early Warning Score 2 (NEWS2), than with influenza type or traditional host risk factors. The use of NEWS2 may support early risk stratification and escalation planning in patients with influenza CAP. Haemophilus influenzae co-detection was associated with lower adjusted odds of severe influenza, which may reflect differences in host airway microbiota rather than a protective bacterial effect.

BACKGROUND

Adults hospitalised with CAP due to influenza may experience rapid clinical deterioration, often requiring oxygen therapy, ventilatory support, or admission to critical care. Early risk stratification is crucial for timely monitoring and escalation of care. However, it remains unclear whether severe influenza is more accurately predicted by host susceptibility, clinical management, or pathogen-related factors such as influenza type.[1] This study aimed to identify predictors of severe influenza among hospitalised adults in a multicentre cohort in Singapore.

METHODS

Adults aged ≥21 years with acute moderate-to-severe CAP were enrolled from four hospitals in Singapore as part of the RESPIRO cohort.[2] Pathogens were identified from clinical specimens using the BioFire® FilmArray® Pneumonia Panel, the Anyplex II RV16 detection kit (Seegene) for respiratory viruses, and routine microbiological investigations. Demographic and clinical data were compared using standard statistical methods. Severe illness was defined as any requirement for supplemental oxygen, high-flow nasal oxygen (HFNO), invasive mechanical ventilation (IMV), or intensive care unit or high-dependency unit (ICU/HDU) care during hospitalisation. Multivariable logistic regression estimated adjusted odds ratios (aORs) with 95% confidence intervals (CIs) for severe illness.

RESULTS

- A total of 168 patients were diagnosed with influenza-associated community-acquired pneumonia (CAP), including 154 with influenza A and 14 with influenza B.
- Severe illness occurred in 87 patients.
- Twenty-three patients required ICU admission: 18 with influenza A and 5 with influenza B.
- After adjusting for age, vaccination status, and comorbidities, influenza type was not significantly associated with severe disease (aOR 0.87, 95% CI 0.27–2.82; p=0.813).
- Age, smoking status, and comorbidities were not independently associated with disease severity.
- A higher National Early Warning Score 2 (NEWS2) at presentation independently predicted severe influenza (aOR 1.84 per 1-point increase, 95% CI 1.53–2.29; p<0.0001).
- In influenza cases with sputum or endotracheal aspirates tested using the BioFire® FilmArray® Pneumonia Panel (n=109), co-detection of H. influenzae (n=40) was associated with lower adjusted odds of severe influenza (aOR 0.31, 95% CI 0.13-0.74; p=0.008) (Figure 2).
- Patients with influenza–H. influenzae co-detection exhibited higher neutrophil counts (median 9.3 vs 6.0 × 10^9/L, p<0.0001) and C-reactive protein levels (168 vs 97 mg/L, p=0.022) at admission.

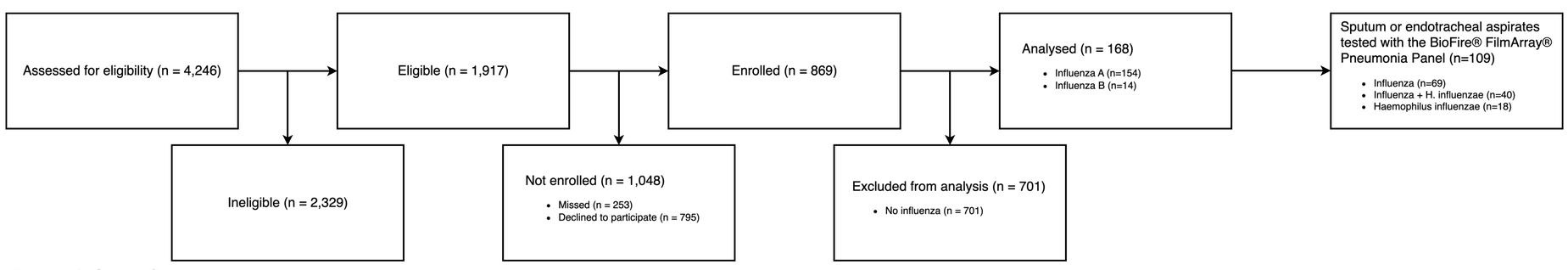

Figure 1. Study flow chart.
A total of 168 adults hospitalised with influenza-associated community-acquired pneumonia were included in this analysis. Of these patients, 154 were diagnosed with influenza A and 14 with influenza B. Among the 109 patients tested with a multiplex pneumonia panel, Haemophilus influenzae was co-detected in 40 cases.

Table 1. Baseline characteristics and clinical outcomes of adults hospitalised with influenza A or B.

Characteristic	Influenza A (n=154)	Influenza B (n=14)	p-value
Demographics			
Age (median, IQR)	66 (58.2-76)	51.5 (41.2-62.8)	0.002
Sex at birth (male, n (%))	90 (58.4%)	9 (64.3%)	0.781
Current smoker	29 (21%)	3 (21.4%)	1.00
Influenza vaccination (within the past year)	18 (11.7%)	1 (7.1%)	1.00
Age-adjusted Charlson comorbidity index	3 (2-4)	2 (0.2-3)	0.078
Interventions			
Supplemental oxygen	80 (51.9%)	7 (50%)	1.00
HFNO	26 (16.9%)	5 (35.7%)	0.140
IMV	11 (7.1%)	3 (21.4%)	0.097
ICU	18 (11.7%)	5 (35.7%)	0.027
HDU	20 (13%)	1 (7.1%)	1.00

P values were calculated using the χ^2 test for categorical variables and the Kruskal–Wallis test for continuous variables. Abbreviations: IQR=interquartile range.

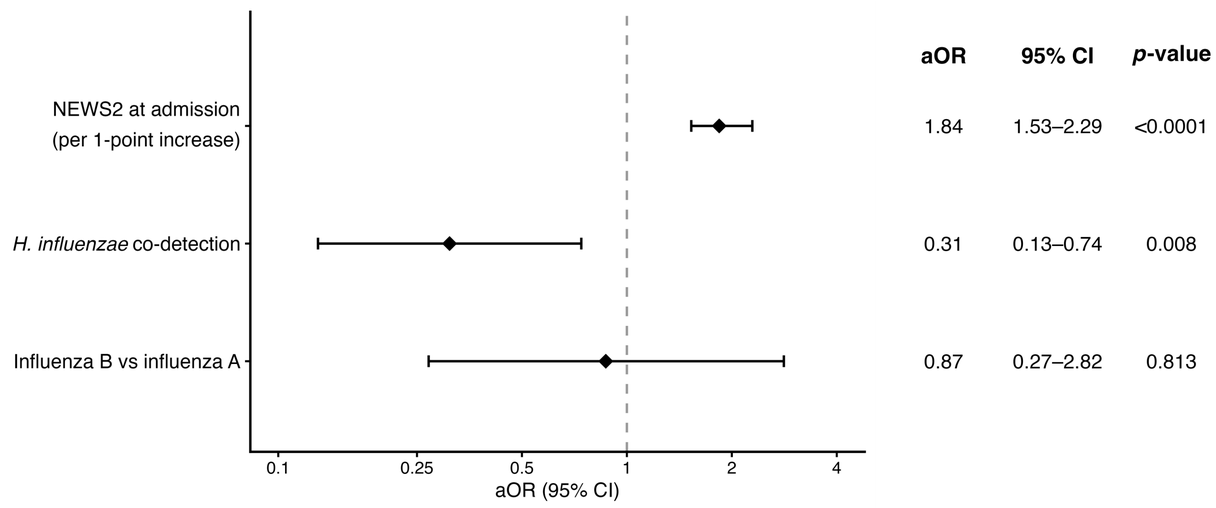

Figure 2. Adjusted predictors of severe influenza.
Forest plot presenting aORs and 95% CIs derived from multivariable logistic regression models evaluating three primary predictors of severe influenza: NEWS2 at presentation, *H. influenzae* co-detection, and influenza B compared with influenza A. Models included patients with influenza A or influenza B (n=165). The *H. influenzae* model was restricted to cases in which sputum or endotracheal aspirates were tested using the BioFire® FilmArray® Pneumonia Panel (n=109).

Table 2. Baseline characteristics and clinical outcomes among patients with influenza without H. influenzae, influenza with H. influenzae, and H. influenzae-only community-acquired pneumonia.

Characteristic	Influenza (n=69)	Influenza + H. influenzae (n=40)	Haemophilus influenzae (n=18)	p-value
Demographics				
Age (median, IQR)	63 (53-73)	67.5 (60.5-76)	72 (61.25-79)	0.071
Sex at birth (male, n (%))	43 (62.3%)	22 (55%)	10 (55.6%)	0.716
Current smoker	19 (29.7%)	4 (11.1%)	3 (17.7%)	0.082
Influenza vaccination (within the past year)	4 (5.8%)	7 (17.5%)	4 (22.2%)	0.040
Age-adjusted Charlson comorbidity index	3 (2-4)	3 (2-4)	3 (2-6)	0.644
Full blood count				
White blood cell count	7.7 (5.3-11.4)	11.4 (7.3-15.0)	13.8 (12.8-14.7)	<0.001
Neutrophils	6 (4.0-9.2)	9.3 (5.4-12.1)	11.3 (9.4-12.1)	<0.001
Lymphocytes	0.9 (0.6-1.3)	1.1 (0.8-1.8)	1.4 (1.0-1.8)	0.005
Monocytes	0.7 (0.5-0.9)	0.9 (0.6-1.3)	1.2 (1.0-1.4)	<0.001
Inflammatory markers				
CRP	97 (41-152.5)	167.8 (67.4-267.6)	145.5 (115.8-193.8)	0.022
Interventions				
Supplemental oxygen	43 (62.3%)	14 (35%)	7 (38.9%)	0.013
HFNO	15 (21.7%)	4 (10%)	0 (0%)	0.036
IMV	5 (7.25%)	2 (5%)	0 (0%)	0.760
ICU	11 (15.9%)	2 (5%)	0 (0%)	0.074
HDU	9 (13%)	3 (7.5%)	0 (0%)	0.272

P values were calculated using the χ^2 test for categorical variables and the Kruskal–Wallis test for continuous variables.

DISCUSSION

The results support the use of early physiological assessment at admission for risk stratification, rather than relying solely on influenza type or traditional host risk factors. NEWS2 at presentation showed the strongest association with severe influenza and may help identify patients who require closer monitoring or earlier escalation of care. In contrast, influenza type, age, smoking status, and comorbidities were not independently associated with severity, although ICU admissions occurred in both influenza A and B groups. An inverse association was observed between H. influenzae co-detection and severe influenza, despite elevated inflammatory markers at admission. However, molecular detection in respiratory specimens may indicate airway carriage rather than true lower respiratory tract infection.[3] This observation may therefore result from differences in host airway microbial profiles, colonisation patterns, or sampling methodologies, rather than a protective bacterial effect, and requires validation in larger international cohorts. Overall, early clinical assessment and improved understanding of the host airway microbiome may provide greater utility for risk-stratifying severe influenza than influenza type alone.

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