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Incidence and Risk Factors of Pneumonia in Hospitalized Patients with Seasonal Influenza A or B

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Background: Most patients with influenza recover spontaneously or following treatment with an anti-viral agent, but some patients experience pneumonia requiring hospitalization. We conducted a retrospective review to determine the incidence and risk factors of pneumonia in hospitalized patients with influenza A or B.

Methods: A total of 213 patients aged 18 years or older and hospitalized with influenza between January 2012 and January 2015 were included in this study. A reverse-transcriptase polymerase chain reaction assay was used to detect the influenza A or B virus in the patients' sputum samples. We collected demographic and laboratory data, combined coexisting diseases, and radiologic findings.

Results: The incidence of pneumonia was higher in patients in the influenza A group compared to those in the influenza B group (68.6% vs. 56.9%), but this difference was not statistically significant. The presence of underlying respiratory disease was significantly associated with pneumonia in the influenza A group (adjusted odds ratio [OR], 3.975; 95% confidence interval [CI], 1.312–12.043; p=0.015). In the influenza B group, the white blood cell count (adjusted OR, 1.413; 95% CI, 1.053–1.896; p=0.021), platelet count (adjusted OR, 0.988; 95% CI, 0.978–0.999; p=0.027), and existence of an underlying medical disease (adjusted OR, 15.858; 95% CI, 1.757–143.088; p=0.014) were all significantly associated with pneumonia in multivariate analyses.

Conclusion: The incidence of pneumonia was 65.7% in hospitalized patients with influenza A or B. The risk factors of pneumonia differed in hospitalized patients with influenza A or B.

Keywords: Pneumonia; Influenza; Risk Factors; Comorbidity

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Introduction

Influenza is a type of self-limiting disease characterized by acute onset of fever, sore throat, malaise, and respiratory symptoms. In healthy people, the disease resolves without any complications. However, considerable excess mortality is observed in elderly and comorbid patients[1]. Although influenza combined with pneumonia can lead to death, mortality is often caused by the aggravation of a preexisting disease such as bronchial asthma, chronic obstructive airways disease, and cardiovascular diseases[2-4].

In the case of seasonal influenza, approximately 1% of hospitalized patients with combined influenza and pneumonia died between 2005 and 2008[5]. From the 1976–1977 to the 2002–2003 seasons, 9.9 deaths per 100,000 attributed to

influenza-associated respiratory and circulatory deaths were reported in the United States[6]. Murata et al.[7] showed that 52% and 17% of 193 patients admitted with influenza A had new infiltrations and definite pneumonia based on chest postero-anterior radiographs, respectively, between 1999 and 2003. Among 35 patients with seasonal influenza admitted to the hospital during the 1999–2000 season, 48.5% were found to have pneumonia[8]. In the United States, the total direct annual cost of influenza has been estimated at US $1–3 billion[9]. These findings suggest that influenza-associated pneumonia could be a problem in the management of influenza itself and also create a social and economic burden.

Many studies have investigated the risk factors related to the clinical course and development of influenza. Some studies have shown that obesity and underlying metabolic diseases worsen the clinical course of pandemic influenza[10,11]. One study cited obesity as a common morbidity for critically ill patients with pandemic influenza in intensive care[12]. Another study showed that asthma was the most common comorbidity in pandemic influenza[13], whereas Jain et al.[14] demonstrated that neurological disease was more associated with influenza than respiratory diseases such as asthma or chronic obstructive pulmonary disease (COPD).

In addition, there are many reports on the incidence and risk factors of pneumonia associated with pandemic influenza, but only a few have noted the risk factors of pneumonia-associated seasonal influenza worldwide. Old age more than 75 years old, white race, chronic lung diseases, and immunosuppression were important risk factors in United States[15]. At recent, the article related with risk factors of pneumonia in 327 Korean patients with seasonal influenza who were managed at outpatient department and hospital was published[16]. They found, also, old age, lung diseases, and other chronic diseases are important risk factors. To the best of our knowledge, there were a few study has addressed the incidence and risk factors of pneumonia in hospitalized patients with seasonal influenza in Korea. In the present study, we investigated the incidence and risk factors of pneumonia in hospitalized patients with seasonal influenza A or B in Korea between 2012 and 2015.

Materials and Methods

1. Inclusion criteria and definitions

This retrospective observational study was performed according to the guidelines of the Declaration of Helsinki and was approved by the local ethics committees (SCHUH-2016-10-010). Patients admitted between January 2012 and June 2015 who met the following criteria were included: age over 18 years old; chest radiographs obtained within 24 hours of hospital admission; and influenza A or B infection confirmed by a reverse-transcriptase polymerase chain reaction (RT-PCR) assay from nasopharyngeal aspirates or sputum. Pneumonia was defined radiographically by the modified World Health Organization criteria as the presence of a consolidation, infiltrate, or opacity that could be described as alveolar, interstitial, or lobar[14].

2. Data

Patients' demographic data, vital signs, clinical manifestations, coexisting conditions, and laboratory and radiographic findings were collated from medical records. Body mass index (BMI; weight in kilograms divided by the square of the height in meters) was calculated to determine whether the patient was overweight or obese, defined as a BMI ≥25 or ≥35, respectively[17]. We analyzed the CURB-65 and CRB-65 scores to determine the severity of pneumonia. The CURB-65 parameter consists of five risk factors, as follows: confusion of new onset, blood urea nitrogen (BUN) greater than 7 mmol/L (19 mg/dL), respiratory rate of 30 breaths per minute or greater, blood pressure less than 90 mm Hg systolic or a diastolic blood pressure 60 mm Hg or less, and an age of 65 years or older. The CRB-65 parameter is as described above but omits the BUN score.

3. Underlying medical conditions

Data were collected on the following underlying medical conditions: gastrointestinal disease including liver cirrhosis, chronic hepatitis, and inflammatory bowel disease; cardiologic disease including heart failure and coronary artery disease; respiratory disease including asthma, COPD, and idiopathic pulmonary fibrosis (IPF); renal disease including chronic kidney disease and end-stage renal disease with dialysis; neurological disease including cerebral infarction, cerebellar infarction, and intracranial hemorrhage; malignancy; and history of transplantation. Hypertension was excluded a cardiologic disease.

4. AdvanSure RV real-time RT-PCR

Nucleic acids (RNA and DNA) were extracted from 200 μL nasopharyngeal samples using a fully automated magnetic bead operating platform, the Smart LabAssist-32 with the TANBead Viral Auto Plate (96-well plate) (Taiwan Advanced Nanotech Inc., Taoyuan City, Taiwan). AdvanSure RV real-time kits (LG Life Sciences, Seoul, Korea) were used to detect 12 types of RNA virus and two types of DNA virus according to the manufacturer's instructions. Briefly, 5 μL extracted nucleic acids was added to an AdvanSure RV real-time RT-PCR reaction tube containing 5 μL primer probe mixture and 10 μL 1-step premix to perform DNA synthesis and real-time RT-PCR. For the reverse transcription step, this mixture was incubated at 50°C for 10 minutes. Denaturation followed at

95°C for 30 seconds, then 10 cycles of polymerase chain reaction (PCR) (15 seconds at 95°C, 30 seconds at 53°C, and 30 seconds at 60°C), followed by 30 additional cycles of PCR to detect fluorescence signals (15 seconds at 95°C, 30 seconds at 53°C, and 30 seconds at 60°C). The AdvanSure RV real-time RT-PCR performed both the reverse-transcription reaction with the extracted RNA and the multiplex PCR reaction simultaneously in a single tube and used endogenous RNase P as an internal control to provide information on the validity of the RNA extraction procedure and to prevent inaccuracies arising from sampling errors and RT-PCR reaction errors.

5. Statistical analysis

Continuous variables are presented as mean±standard deviation, or as medians with ranges. Categorical variables are presented as numbers and percentages. Multivariate analyses was performed to compare the clinical characteristics of patients with seasonal influenza and co-infected pneumonia. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. p-values were calculated using the chi-square test or Fisher exact test for categorical variables, as appropriate, and by the Student's t test or Mann-Whitney U test for continuous variables. The clinical findings, laboratory findings, and underlying medical conditions were analyzed as variables for independent risk factors of the incidence of pneumonia in each group. Variables for which the p-value was <0.2 in univariate analyses were included in a logistic regression model for multivariate analyses. Variable selection was performed by backward method. All tests were two-tailed, and a p-value of <0.05 was considered to indicate significance in the multivariate model. All analyses were performed with SPSS version 15.0 (SPSS Inc., Chicago, IL, USA).

Results

1. Baseline characteristics

Data from 216 patients infected with the influenza A or B virus were available for analysis. Three patients were excluded due to being positive for both viruses. A total of 210 patients were subsequently evaluated and the clinical characteristics of 159 patients with influenza A (74.6%) and 51 patients with influenza B (25.4%) are presented in Table 1. The patients' clinical characteristics, including underlying medical conditions, did not differ between the two groups. Diabetes mellitus was the most common comorbidity in both groups (Table 1).

2. Incidence of pneumonia

The incidence of pneumonia in the influenza A group was higher compared to the influenza B group (68.6% vs. 56.9%) but the difference was not statistically significant (p=0.126), with both groups together having an incidence of 65.7% (Table 1).

3. Laboratory and clinical findings

Among the patients hospitalized with the influenza A virus, female patients were more predominant in the pneumonia group (56.9%) compared to the non-pneumonia group (38.0%) (p<0.05). Respiratory diseases were more common in the pneumonia group (25.7%) than in the non-pneumonia group (8.0%) (p=0.01). Laboratory findings, other clinical findings, and underlying medical diseases did not differ between the groups except for the CRB-65 score (Table 2).

Among the patients hospitalized with influenza B, pa-

Table 1. Baseline characteristics of patients with influenza A or B

Characteristic	Influenza A virus (n=159)	Influenza B virus (n=51)	Total (n=210)
Male sex	81 (50.9)	23 (45.1)	104 (49.5)
Age, yr	68 (19–95)	69 (24–91)	68 (19–95)
Pneumonia	109 (68.5)	29 (56.9)	138 (65.7)
Underlying medical conditions			
Gastrointestinal diseases	23 (14.5)	5 (9.8)	28 (13.3)
Cardiologic diseases	35 (22.0)	10 (19.6)	45 (21.4)
Respiratory diseases	32 (20.1)	15 (29.4)	47 (22.4)
Diabetes mellitus	49 (30.8)	18 (35.3)	67 (31.9)
Malignancies	38 (23.9)	11 (21.6)	49 (23.3)
Renal diseases	20 (12.6)	12 (23.5)	32 (15.2)
Transplantation	1 (0.6)	1 (2.0)	2 (1.0)
Neurological diseases	14 (8.8)	8 (15.7)	22 (10.5)

Values are presented as number (%) or median (range).

Table 2. Laboratory and clinical findings of patients with influenza A

Variable	Non-pneumonia (n=50)	Pneumonia (n=109)	p-value
Demographics			
Female sex	19 (38.0)	62 (26.9)	0.028
Age, yr	63.5±18.1	66.0±16.5	0.193
Laboratory finding			
WBC count, $\times 10^3/\mu L$	7.61±4.49	8.36±5.55	0.204
Hemoglobin, g/dL	10.9±1.97	10.79±1.94	0.329
Hematocrit, %	32.88±5.85	32.75±5.75	0.448
Platelet count, $\times 10^3/\mu L$	201.48±103.12	188.48±91.40	0.410
AST, U/L	37.44±50.10	59.56±190.97	0.223
ALT, U/L	30.06±34.15	44.94±144.68	0.295
BUN, mg/dL	20.50±17.99	20.19±17.00	0.021
Serum creatinine, mg/dL	1.89±2.65	1.45±2.02	0.137
eGFR, mL/min	71.65±37.05	75.78±32.48	0.476
CRP, mg/dL	6.23±7.91	8.43±8.52	0.124
CURB-65 score	1.20±1.05	1.36±1.10	0.221
CRB-65 score	0.82±0.77	1.02±0.86	0.099
Clinical finding			
Respiratory rate	19.22±4.16	19.58±3.60	0.311
Systolic blood pressure, mm Hg	121.76±22.38	118.46±19.04	0.171
Diastolic blood pressure, mm Hg	71.32±11.27	70.02±10.24	0.239
Height, cm	158.48±9.20	160.72±10.94	0.049
Weight, kg	60.88±12.70	60.01±11.82	0.336
BMI	24.13±4.04	23.25±4.17	0.310
Body temperature, °C	36.84±0.68	36.86±0.68	0.438
Pulse rate	79.24±10.07	82.94±17.89	0.087
Abnormal mental status	3 (6.0)	15 (13.8)	0.153
Underlying medical conditions			
Hypertension	20 (40.0)	53 (48.6)	0.312
Diabetes	15 (30.0)	34 (31.2)	0.880
Respiratory disease	4 (8.0)	28 (25.7)	0.010
Gastrointestinal disease	6 (12.0)	17 (15.6)	0.551
Cardiologic disease	12 (24.0)	23 (21.1)	0.683
Malignancy	9 (18.0)	29 (26.6)	0.221
Renal disease	6 (12.0)	14 (12.8)	0.882
Transplantation	1 (2.0)	0	0.140
Neurological disease	3 (6.0)	11 (10.1)	0.399
No underlying disease	11 (22.0)	19 (17.4)	0.496

Values are presented as number (%) or median (range).
WBC: white blood cell count; AST: aspartate aminotransferase; ALT: alanine aminotransferase; BUN: blood urea nitrogen; eGFR: estimated glomerular filtration rate; CRP: C-reactive protein; BMI: body mass index.

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Table 3. Laboratory and clinical findings of patients with influenza B

Variable	Non-pneumonia (n=22)	Pneumonia (n=29)	p-value
Demographics			
Female sex	12 (54.5)	16 (55.2)	0.965
Age, yr	61.9±17.0	69.0±12.8	0.048
Laboratory findings			
WBC count, $\times 10^3/\mu L$	5.95±3.17	7.48±3.32	0.049
Hemoglobin, g/dL	11.85±2.09	11.31±1.93	0.174
Hematocrit, %	35.37±6.01	34.20±5.38	0.233
Platelet count, $\times 10^3/\mu L$	180.36±85.14	134.97±68.77	0.021
AST, U/L	29.68±22.07	26.72±17.01	0.303
ALT, U/L	26.73±21.56	24.24±23.50	0.351
BUN, mg/dL	14.46±14.34	17.44±8.91	0.192
Serum creatinine, mg/dL	0.92±0.87	1.19±0.98	0.169
eGFR, mL/min	90.19±23.89	72.67±27.91	0.010
CRP, mg/dL	3.35±5.79	4.77±5.43	0.190
CURB-65 score	1.05±1.09	1.55±1.33	0.074
CRB-65 score	0.91±0.92	1.14±0.92	0.234
Clinical findings			
Respiratory rate	19.73±2.16	20.31±2.92	0.236
Systolic blood pressure, mm Hg	113.59±10.92	118.07±12.17	0.092
Diastolic blood pressure, mm Hg	68.77±9.06	70.21±8.65	0.289
Height, cm	163.00±11.17	160.20±8.81	0.161
Weight, kg	63.13±13.26	59.92±12.17	0.186
BMI	23.60±3.44	23.26±3.67	0.062
Body temperature, °C	37.00±0.78	36.72±0.66	0.085
Pulse rate	85.59±14.04	81.93±9.86	0.151
Abnormal mental status	1 (4.5)	6 (20.7)	0.100
Underlying medical conditions			
Hypertension	10 (45.5)	18 (62.1)	0.242
Diabetes	8 (36.4)	10 (34.5)	0.890
Respiratory disease	4 (18.2)	11 (37.9)	0.129
Gastrointestinal disease	2 (9.1)	3 (10.3)	0.883
Cardiologic disease	3 (13.6)	7 (24.1)	0.354
Malignancy	5 (22.7)	6 (20.7)	0.915
Renal disease	5 (22.7)	7 (24.1)	0.907
Transplantation	1 (4.5)	0	0.251
Neurological disease	2 (9.1)	6 (20.7)	0.264
No underlying disease	7 (31.8)	2 (6.9)	0.022

Values are presented as number (%) or median (range).
WBC: white blood cell count; AST: aspartate aminotransferase; ALT: alanine aminotransferase; BUN: blood urea nitrogen; eGFR: estimated glomerular filtration rate; CRP: C-reactive protein; BMI: body mass index.

tients in the pneumonia group were older than those in the non-pneumonia group (69.0±12.8 years vs. 61.9±17.0 years, p<0.05). In contrast to the influenza A group, the incidence of underlying respiratory disease did not differ between the pneumonia and non-pneumonia groups. The pneumonia group had a higher white blood cell (WBC) count than the non-pneumonia group (5.950±3.170/μL vs. 7.480±3.320/μL, p=0.049) (Table 3).

4. Risk factors for pneumonia

To identify the factors associated with the incidence of pneumonia in hospitalized patients with influenza, each group was investigated using multivariate analyses. Sex, heart rate, abnormal mental status, C-reactive protein, underlying respiratory diseases, and the CRB-65 score were all associated with the incidence of pneumonia in the influenza A group. Among them, underlying respiratory diseases were significantly associated with pneumonia in multivariate analyses (adjusted OR, 3.975; 95% CI, 1.312–12.043; p=0.015) (Table 4).

With regard to the influenza B group (Table 5), an age over 65 years old, body temperature, systolic blood pressure, abnormal mental status, WBC count, platelet count, estimated glomerular filtration rate, the existence of an underlying medical condition, underlying respiratory diseases, and the CURB-65 score were all associated with the incidence of pneumonia. Among them, the WBC count (adjusted OR, 1.413; 95% CI, 1.053–1.896; p=0.021), platelet count (adjusted OR, 0.988; 95% CI, 0.978–0.999; p=0.027), and the existence of an underlying medical disease (adjusted OR, 15.858; 95% CI, 1.757–143.088; p=0.014) were significantly associated with pneumonia in multivariate analyses. In contrast to the influenza A group, underlying respiratory diseases were not significantly associated with pneumonia (Table 5).

While various findings were associated with the incidence of pneumonia in the total group of patients, only underlying respiratory diseases had a significant association (adjusted OR, 3.155; 95% CI, 1.347–7.387; p=0.008) (Table 6).

Table 4. Risk factors of the incidence of pneumonia in hospitalized patients with influenza A

Variable	Univariate			Multivariate		
	OR	95% CI	p-value	Adjusted OR	95% CI	p-value
Female sex	0.465	0.234–0.922	0.028	-	-	-
Heart rate	1.016	0.992–1.041	0.180	-	-	-
Abnormal mental status	2.500	0.689–9.065	0.163	-	-	-
CRP, mg/dL	1.036	0.990–1.083	0.128	-	-	-
Respiratory diseases	3.975	1.312–12.043	0.015	3.975	1.312-12.043	0.015
CACI	1.142	0.980–1.330	0.088	-	-	-
CRB-65	1.334	0.884–2.047	0.166	-	-	-

OR: odds ratio; CI: confidence interval; CRP: C-reactive protein; CACI: Charlson Age-Comorbidity Index.

Table 5. Risk factors of the incidence of pneumonia in hospitalized patients with influenza B

Variable	Univariate			Multivariate		
	OR	95% CI	p-value	OR	95% CI	p-value
Age ≥65 yr	1.034	0.994–1.077	0.100	-	-	-
Body temperature	0.567	0.249–1.289	0.175	-	-	-
Systolic blood pressure, mm Hg	1.035	0.984–1.088	0.180	-	-	-
Abnormal mental status	5.478	0.608–49.348	0.129	-	-	-
WBC count, $\times 10^3/\mu L$	1.173	0.964–1.426	0.111	1.413	1.053–1.896	0.021
Platelet count, $\times 10^3/\mu L$	0.992	0.984–1.000	0.047	0.988	0.978–0.999	0.027
eGFR, mL/min	0.971	0.945–0.998	0.035	-	-	-
Existence of underlying condition	6.300	1.158–34.262	0.033	15.858	1.757–143.088	0.014
Respiratory diseases	2.750	0.736–10.271	0.132	-	-	-
CURB-65 score	1.521	0.895–2.584	0.121	-	-	-

OR: odds ratio; CI: confidence interval; WBC: white blood cell count; eGFR: estimated glomerular filtration rate.

Table 6. Risk factors of the incidence of pneumonia in hospitalized patients with both influenza A and B

Variable	Univariate			Multivariate		
	OR	95% CI	p-value	Adjusted OR	95% CI	p-value
Female sex	0.567	0.318–1.010	0.054	-	-	-
Abnormal mental status	3.051	1.005–9.261	0.049	-	-	-
WBC count, $\times 10^3/\mu L$	1.051	0.985–1.122	0.133	-	-	-
Platelet count, $\times 10^3/\mu L$	0.998	0.995–1.001	0.189	-	-	-
CRP, mg/dL	1.042	1.000–1.086	0.048	1.047	1.005–1.091	0.028
Type of virus	0.605	0.316–1.155	0.128	-	-	-
Respiratory diseases	3.152	1.384–7.178	0.006	3.399	1.483–7.793	0.004
CURB-65	1.235	0.944–1.617	0.124	-	-	-
CRB-65	1.321	0.934–1.868	0.116	-	-	-
CACI	1.137	1.000–1.293	0.050	-	-	-

OR: odds ratio; CI: confidence interval; WBC: white blood cell count; CRP: C-reactive protein; CACI: Charlson Age-Comorbidity Index.

Discussion

Infection with the influenza virus can lead to various complications. However, among them, the occurrence of pneumonia has been considered a serious condition that should be treated properly because it can lead to death. Riquelme et al.[18] demonstrated that more severe respiratory compromise was found in patients with pneumonia associated with pandemic influenza A (H1N1) compared to those with seasonal influenza. Another report showed that patients hospitalized with pandemic influenza A (H1N1) were more likely to have complications such as lower respiratory tract infections, shock or sepsis, and organ failure compared to those with seasonal influenza[19]. However, nearly one-third of patients with seasonal influenza in the United States had pneumonia and this was associated with admission to an intensive care unit and death[15]. For this reason, we speculated that seasonal influenza can cause severe respiratory complications and even death, although it has a much milder clinical course than pandemic influenza. We investigated the incidence and risk factors of pneumonia in hospitalized patients with seasonal influenza in Korea. The incidence was 68.6%, 56.9%, and 65.7% in influenza A, influenza B, and influenza A and B combined, respectively. In the United States, a recent epidemiologic study reported that 29% of patients had pneumonia among 4,765 patients hospitalized with influenza[15]. However, a separate study showed that 48.5%–52% of patients hospitalized with influenza had pneumonia[7,8]. This large difference may be related to the type of hospital and difficulty admitting patients. Because present study was performed at a tertiary hospital in Seoul, it was not easy to admit patients with mild symptoms. Furthermore, no epidemiologic studies to date have included admission criteria. This suggests that prospective studies are required to define the incidence of pneumonia in hospitalized patients with influenza.

Complicated influenza infections are associated with obesity, underlying pulmonary disease, cardiologic disease, and old age[10,11,20]. Our findings are consistent with this, in that the main risk factors for pneumonia were respiratory disease and underlying medical conditions in patients with influenza A and B, respectively. Other factors such as the WBC and platelet counts were risk factors for pneumonia in patients with influenza B, which was not found in other pandemic studies. This difference may be explained by the different target populations: seasonal influenza in our study and pandemic influenza in other studies. Hong et al.[21] showed that the main risk factor for complicated seasonal influenza was diabetes mellitus. In our study, although diabetes mellitus was the most common underlying medical condition, diabetes itself did not serve as a risk factor for pneumonia.

It is widely accepted that influenza B viruses are more likely to infect children and cause milder illness than influenza A viruses[22]. Furthermore, influenza A and B affect different segments of the population. Older age is associated with increased influenza A detection[23]. Thus, we compared the incidence and risk factors of pneumonia in both influenza A and B. The incidence of pneumonia was similar between the influenza A and B groups. We are unable to explain this difference. Future studies that include virology data are needed to clarify this difference.

The present study had several limitations. First, it was performed at a single center with a relatively small study population. Second, we did not analyze subtypes of the influenza virus. However, the subtypes of seasonal influenza do not alter treatment regimens or have clinical implications. Third, we were unable to differentiate the cause of pneumonia as either primary viral pneumonia or secondary bacterial pneumonia because, clinically, it is very difficult to isolate the infectious

agents. Fourth, we did not define indications of hospitalization. However, most previous epidemiologic studies also did not do this due to their retrospective design.

In conclusion, the incidence of pneumonia was 65.7% in patients hospitalized with influenza, and underlying respiratory disease (e.g., asthma, COPD, and IPF) was a strong risk factor for the incidence of pneumonia in hospitalized patients with influenza A. Otherwise, the existence of an underlying disease along with laboratory findings such as elevated WBC and platelet counts are significantly associated with pneumonia in patients with influenza B.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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