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Main Clinical Characteristics of Patients Admitted to the Hospital for Influenza During the Last Two Seasons and Risk Factors for Severity According to the Vaccination Status

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Abstract

Background/Objectives: Few data exist on clinical characteristics of patients admitted to the hospital for influenza and risk factors associated with its severity. **Methods**: We retrospectively collected data on patients admitted for influenza in Cannes Hospital, France, during the 2024–2025 and 2025–2026 seasonal outbreaks. Severe forms were defined as cases either requiring admission to the Intensive Care Unit (ICU) or resulting in death. They were compared to uncomplicated forms. The main demographic, clinical, radiological, and laboratory characteristics were collected for each patient, together with their vaccination status. **Results**: From October 2024 to May 2026, we included 105 subjects (mean age 72 years, 57% male, 39% vaccinated, 96% with type A influenza, 53% with two or more comorbid conditions, 31% admitted to ICU, and 15% deaths). Although vaccinated subjects were older and had a similar incidence of pneumonia as unvaccinated individuals, they had lower rates of severe forms and a better chance of survival ($p < 0.05$ for both). Compared to uncomplicated cases, those with severe forms had: higher rates of pneumonia, acute renal failure, and treatment with oseltamivir; higher neutrophil/lymphocyte ratio and C-reactive protein values at admission; and lower vaccination coverage. In multivariate analysis, vaccination status, treatment with oseltamivir, and the neutrophil/lymphocyte ratio were independent predictors of clinical severity ($p < 0.05$ for all). **Conclusions**: Vaccinated subjects had fewer severe forms than unvaccinated individuals despite their older age, and vaccination status was a predictive factor for clinical severity together with the neutrophil/lymphocyte ratio.

Keywords: influenza; hospitalization; severity; vaccination

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1. Introduction

Each year, seasonal influenza is a major cause of acute respiratory tract infections worldwide [1–3]. While uncomplicated cases in younger patients lead to a socioeconomic burden mainly driven by absenteeism costs [4], hospitals annually face seasonal influenza outbreaks, especially among the most fragile subjects, such as elderly patients and those with comorbid conditions, with a massive impact on public health [5–10]. Indeed, it is established that influenza causes up to 650,000 deaths annually worldwide, with the highest rates of severity and mortality among patients older than 75 and/or with comorbidities [11,12].

Reducing disease severity and consequently hospital admissions is therefore a priority, with annual influenza vaccination representing a cornerstone of prevention [13,14].

However, the effects of vaccination vary from year to year, and breakthrough infections in vaccinated subjects are not rare [15,16]. Moreover, the majority of studies on vaccine efficacy are limited to outpatients or are epidemiological studies on subjects admitted to the hospital [17–19]. Few studies describe the characteristics of inpatients from the clinical point of view and analyze risk factors associated with severe forms [20,21].

The aim of this study was to describe the main clinical, radiological, and laboratory characteristics of vaccinated and unvaccinated patients with influenza admitted to the hospital during the last two seasons and to analyze risk factors associated with severity.

2. Materials and Methods

2.1. Study Design and Participants

We performed a retrospective observational study on patients admitted to Cannes General Hospital with influenza infection during the 2024–2025 and 2025–2026 seasons, aiming to report their main clinical, radiological, and laboratory characteristics. In particular, the main goals were to describe the characteristics of vaccinated and unvaccinated subjects and to explore risk factors associated with severe forms, defined by either admission to the Intensive Care Unit or death. Data from each subject were extracted from the hospital electronic database.

Each subject received a notification letter informing them that their data would be collected anonymously for the purpose of the study, unless the individual refused, to ensure privacy.

The following parameters were collected: main demographic characteristics; number and type of comorbid conditions; vaccination status and type of vaccination against influenza; body mass index (BMI); types and subtypes of influenza strains when available; symptom duration; clinical signs upon admission and during hospitalization; main laboratory findings at their admission; imaging performed during their hospital stay; type of O_2 therapy required during the hospitalization; management; and clinical outcome. Subjects previously vaccinated in their life but not during the current season of hospital admission were considered as unvaccinated.

We recruited all subjects admitted to the ICU during both seasons, while, among the Departments of Medicine, the Infectious Diseases Department participated in both seasons' collections, and those of pneumology, nephrology, and general medicine only in the 2025–2026 period, thus explaining the larger number of participants in the second season.

As one of the main goals of the study was exploring the role of vaccination on clinical presentation, subjects were excluded in case of lack of information about the vaccination status.

After a description of the population studied, we firstly compared the main characteristics of vaccinated and unvaccinated subjects in order to identify any potential differences.

In particular, we analyzed which type of vaccination they received, distinguishing among high-dose, adjuvanted, and low-dose vaccines, the first two being considered more efficacious and recommended among people older than 65 years or with comorbid conditions [21–23]. Moreover, we analyzed, when available, the interval between the date of vaccination and symptom onset in order to evaluate whether at least 15 days had passed to consider efficacy.

We then compared subjects with severe forms with those presenting with uncomplicated influenza in order to measure any significant difference. As previously mentioned, severe forms were defined as either transfer to the ICU or death.

2.2. Laboratory Markers

The following parameters at admission were extracted from the patients' database: C-reactive protein (CRP), neutrophil and lymphocyte counts, and liver and renal function.

As an elevated neutrophil/lymphocyte ratio (N/L) has been previously shown as a marker of clinical severity, particularly if it is higher than 15, we included such a measurement in the analysis, using this cut-off for the correlations with the clinical presentation [24–26].

Diagnosis of influenza was performed by either a nasal or throat swab, using NeuMoDx™ Flu A-B/RSV/SARS-CoV-2 (Qiagen, Courtaboeuf, France) or Xpert® Xpress CoV-2/Flu/RSV (Cepheid, Maurens-Scopont, France) plus real-time RT-PCR assays.

2.3. Radiological Findings

Chest imaging results, either by radiography or computerized axial tomography, were collected for each patient and analyzed. According to imaging results, patients were categorized as with or without pneumonia.

2.4. Statistical Analysis

The main demographic, laboratory, and clinical characteristics and the outcome were described for the entire population. Categorical variables were illustrated as frequency rates and percentages, while continuous variables were detailed with means, medians, and interquartile range (IQR).

Moreover, comparisons were firstly conducted between vaccinated and unvaccinated patients and secondly between subjects with severe and uncomplicated forms by using either χ^2-tests or Fisher's exact test for qualitative variables and either Student's *t*-tests or the Wilcoxon–Mann–Whitley test for quantitative parameters. The variables with a p-value ≤ 0.20 in the univariate analysis were initially selected for the multivariate model, and only those with a p-value ≤ 0.05 were retained in the final model.

Statistical analyses were performed using the Statview software version 5 (Abacus Concepts, Inc., Berkeley, CA, USA).

2.5. Ethics Statement

All data used in the analysis were collected during routine public health surveillance activities, and data were completely anonymized before analysis. Therefore, data were exempt from institutional board review. According to French law, the study was submitted to the internal register of the Department of Clinical Research at Nice University Hospital (CHC 51-2025-001), and patients received written information about this project.

3. Results

3.1. Characteristics of Patients

From October 2024 to May 2025 and from October 2025 to May 2026, we identified 124 subjects admitted either to the Department of Medicine or the ICU in Cannes General Hospital. Fourteen of them were excluded, as no information was available on vaccination status.

Hence, we analyzed 105 patients (mean age 72 years, 57% male, 39% vaccinated, 96% with type A influenza, 53% with two or more comorbid conditions, 31% admitted to ICU, and 15% who died during the hospital stay; Table 1). The large majority of individuals came from private residences, while very few subjects were admitted from nursing homes. Moreover, main demographic and background characteristics were similar in the two seasons studied. Influenza A strains were typed only in 10 cases, all admitted to the ICU, with six of them presenting the subtype H3N2 and four the subtype H1N1.

Table 1. Characteristics of patients included.

	N (%) or Mean [SD]
Number of patients	105
Male gender	60 (57.1%)
Age (years)	72.5 [15.0]
Provenance	
Private residence	95 (90.4%)
Nursing home	9 (8.6%)
Other	1 (1%)
Body mass index	24.2 [6.0]
Days of symptoms prior to diagnosis	4.3 [3.4]
Comorbid conditions	
Less than 2	49 (46.7%)
Two or more than 2	56 (53.3%)
Influenza season	
2024–2025	42 (40.0%)
2025–2026	63 (60.0%)
Influenza type	
A	101 (96.2%)
B	4 (3.8%)
Influenza vaccination in the current season	41 (39.0%)
Neutrophils/lymphocytes ratio	12.1 [14.2]
Acute renal failure	39 (37.1%)
Acute hepatitis	40 (38.1%)
Pneumonia on chest imaging	53 (50.5%)
Days on O_2 therapy	2.5 [4.3]
Treatment with oseltamivir	81 (77.1%)
Type of O_2 therapy received *	
No O_2	37 (37.0%)
Low-flow O_2	47 (47.0%)
High-flow O_2 or mechanical ventilation	16 (16.0%)
Transfer to Intensive Care Unit	33 (31.4%)
Deaths	16 (15.2%)

SD: Standard deviation; * Information available only for 100 patients.

Among the vaccinated subjects, the mean interval between vaccination and symptom onset was 38 days, with just 5 out of 41 individuals who had been vaccinated within less than 15 days. Although national and international guidelines recommended preferentially either the high-dose or the adjuvanted inactivated vaccines for the large majority of subjects included in the study [11,23,27], only three of them received one of these compounds, and the remaining 38 subjects were vaccinated using the standard-dose compound.

3.2. Differences Between Vaccinated and Unvaccinated Participants

Main characteristics of vaccinated and unvaccinated subjects are presented in Table 2. Vaccinated individuals were older, while the other demographic and background characteristics did not change between the two groups. Moreover, the duration of symptoms before their arrival was similar between the two groups.

Table 2. Differences between vaccinated and not vaccinated subjects.

	Vaccinated N (%) or Mean [SD]	**Unvaccinated N (%) or Mean [SD]**	***p*-Value**
Number of patients	41	64	
Male gender	23 (56.1%)	37 (57.8%)	0.863
Age (years)	79.1 [11.4]	76.0 [15.5]	0.0002
Body mass index	25.3 [5.7]	23.5 [6.2]	0.151
Two or more comorbid conditions	22 (53.7%)	34 (53.1%)	0.957
Days of symptoms at admission	4.0 [3.6]	4.5 [3.3]	0.501
Acute renal failure	13 (31.7%)	26 (40.6%)	0.354
Acute hepatitis	14 (34.1%)	26 (40.6%)	0.659
Baseline C-reactive protein value (mg/L)	86.1 [64.2]	125.4 [106.8]	0.038
Baseline N/L	9.6 [10.9]	13.7 [15.8]	0.150
Baseline P/L	274.0 [224.9]	338.8 [236.4]	0.174
Pneumonia on chest imaging	22 (53.7%)	31 (48.4%)	0.602
Treatment with oseltamivir	33 (80.5%)	48 (75%)	0.511
Severe form	8 (19.5%)	31 (48.4%)	0.002
Maximum l/min levels of low-flow O_2	3.1 [4.0]	3.9 [4.9]	0.408
Noninvasive high-flow O_2	12 (29.2%)	30 (46.9%)	0.070
Transfer to ICU	6 (14.6%)	27 (42.2%)	0.002
Deaths	2 (4.9%)	14 (21.9%)	0.011
Days of hospital stay	9.2 [5.4]	8.2 [6.5]	0.470

N/L: neutrophil/lymphocytes. P/L: platelets/lymphocytes. ICU: Intensive Care Unit. SD: Standard deviation.

Regarding laboratory and radiological findings, vaccinated and unvaccinated individuals had similar parameters, with the exception of lower values of CRP among vaccinated subjects.

Interestingly, despite similar incidence of pneumonia, low-flow oxygen need, and antiviral treatment received, vaccinated subjects had lower rates of transfer to ICU and better survival (Table 2).

3.3. Risk Factors for Severe Forms

Comparison between severe and uncomplicated forms showed as follows: higher rates of pneumonia on chest imaging, acute renal failure, and treatment with oseltamivir; higher

N/L and CRP values at admission; and lower vaccination coverage among subjects with severe forms, despite similar demographic and background characteristics (Table 3).

Table 3. Differences between severe and uncomplicated forms.

	Severe Form N (%) or Mean [SD]	Uncomplicated Form N (%) or Mean [SD]	*p*-Value
Number of patients	39	66	
Male gender	24 (61.5%)	36 (54.5%)	0.483
Age (years)	70.8 [13.2]	73.4 [15.5]	0.392
Body mass index	24.2 [6.2]	24.2 [6.0]	0.995
Influenza season 2024–2025 2025–2026	17 (43.6%) 22 (56.4%)	25 (37.9%) 41 (62.1%)	0.565
Two or more comorbid conditions	20 (51.3%)	36 (54.5%)	0.746
Days of symptoms at admission	3.6 [2.4]	4.7 [3.9]	0.110
Pneumonia on chest imaging	25 (64.1%)	28 (42.4%)	0.030
Acute renal failure	21 (53.8%)	18 (27.2%)	0.007
Acute hepatitis	17 (43.6%)	23 (34.8%)	0.517
Baseline C-reactive protein value (mg/L)	139.7 [111.8]	92.6 [77.9]	0.013
Baseline N/L	17.6 [17.1]	9.0 [11.4]	0.003
Baseline N/L > 15	16 (43.2%)	8 (12.3%)	<0.001
Treatment with oseltamivir	37 (94.5%)	44 (66.7%)	<0.001
Vaccinated for influenza	8 (20.5%)	33 (50.0%)	0.002
Days of hospital stay	9.2 [5.4]	8.2 [6.5]	0.470

N/L: Neutrophil/Lymphocyte ratio.

Multivariate analysis confirmed that the vaccination status, the N/L ratio, and treatment with oseltamivir were independently associated with the clinical presentation; those with uncomplicated forms were more frequently vaccinated, less frequently treated with oseltamivir, and had higher rates of N/L ratio < 15 (Table 4).

Table 4. Independent risk factors associated with clinical severity.

Non-Severe vs. Severe Influenza			
	Adjusted OR	**CI-95%**	***p*-Value**
C-reactive protein	0.995	0.99–1.01	0.111
No acute renal failure	2.56	0.88–7.38	0.083
N/L ratio < 15	7.14	2.01–25.28	0.002
No treatment with oseltamivir	17.00	2.85–101.28	0.002
No influenza vaccination	0.261	0.08–0.83	0.023

N/L: Neutrophils/lymphocytes. OR: Odds Ratio. CI: Confidence Interval.

Mortality between receiving oseltamivir and untreated subjects did not change (17% vs. 8%, $p = 0.257$).

4. Discussion

In the last two influenza seasons in France, we found that vaccinated subjects, despite their older age and similar underlying medical conditions, had less severe forms of influenza than unvaccinated individuals.

These results suggest that influenza vaccination protects against severe forms despite breakthrough infections and confirm its pivotal role in prevention campaigns [28]. Indeed, the major goal of effective vaccines is to attenuate disease severity by pre-existing immunity, especially among the most fragile subjects [15]. Confirming this hypothesis, we found that low-flow oxygen needs and incidence of pneumonia were similar between vaccinated

and unvaccinated subjects, while rates of complications differed, suggesting a more rapid attenuation of symptoms among vaccinated individuals.

However, although national and international guidelines recommend adjuvanted or higher-dose vaccines among fragile individuals, the large majority of patients received the standard vaccination. Previous studies showed that adjuvanted and high-dose vaccines elicit a more robust immune response to influenza among subjects above 65 years old or with comorbidities, with the majority of works converging toward their benefit for preventing hospitalizations [29,30]. Although the study design does not allow us to respond to this question, very few patients were admitted to the hospital after receiving high-immunogenic vaccination, thus suggesting their protective role in preventing hospitalizations. Indeed, the large majority of admissions came from private residences, with very few individuals coming from nursing homes, where policies about boosted vaccinations are generally more widely implemented. Information campaigns to general practitioners and pharmacies about current guidelines for vaccination may therefore reduce the number of admissions for breakthrough infections, but specific studies on this point are necessary.

Moreover, despite the limits of the retrospective character of the study, we confirmed our previous findings that the N/L ratio could be a predictive marker for severity.

As previously shown, this is a simple marker of systemic inflammation combining both innate and adaptive immunity [31]. Indeed, the pro-inflammatory response to the influenza virus is probably fueled by the endothelial cells, which are involved early in the cytokine release and in the recruitment of innate cells to the lung, resulting in potential tissue damage [32–35]. Moreover, neutrophils are able to migrate to lymph nodes, continually crosstalking with lymphocytes and antigen-presenting cells, thus modulating B- and T-cell responses [36]. In addition, lymphocytes could decrease during viral infections by various mechanisms, including cytokine release, cellular apoptosis, and lymphocyte sequestration in lungs, with potentially important consequences for viral clearance [37]. Considering that in some cases signs of severity were not present at the patient's admission but appeared during the hospital stay, such markers could represent an easy-to-perform tool for identifying subjects at higher risk for complicated forms, requiring closer monitoring. However, prospective randomized studies are needed to clarify this point.

Moreover, we found that antiviral treatment with oseltamivir was associated with greater severity. However, although some controversies about its efficacy and even about increased associated mortality have been raised recently [38], the study design does not allow concluding any cause–effect relationship with clinical severity. Indeed, severe patients are obviously more frequently treated with antivirals than those with uncomplicated forms. In addition, in our study, the mean duration of symptoms was 4 days, while oseltamivir is known to be more efficacious when administered in the first 48 h [39]. Moreover, mortality did not differ between treated and untreated subjects.

As inflammation plays a crucial role in severe cases, it has been suggested that adjunctive immunomodulatory therapies rather than antivirals could be useful during influenza infections, but large-scale trials are needed [40].

Other limitations of the study include limited information on subtype distinction between H1N1 and H3N2 and the lack of data about the prevalence of the H3N2 subclade K, which rapidly spread in the Northern Hemisphere and has several mutations on the haemagglutinin surface protein, potentially associated with immune escape [41].

5. Conclusions

In conclusion, we found that vaccinated subjects had less severe forms than unvaccinated individuals despite their older age, and that the vaccination status was a predictive factor for the clinical severity together with the neutrophil/lymphocyte ratio.

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Informed Consent Statement: Patients received written information about the study and gave their consent to participate and to publish these data.

Data Availability Statement: The original contributions presented in this study are included in this article; further inquiries can be made to the corresponding author.

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