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Short Article

Surveillance of hospitalised severe cases of influenza A(H1N1)pdm09 and related fatalities in nine EU countries in 2010–2011

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A few months into the 2009 influenza pandemic, nine European countries implemented case-based surveillance of hospitalised severe influenza infections. In the present study, we assess the association between patient characteristics, in particular underlying conditions, and the severity level of influenza A(H1N1)pdm09 infection during the 2010-2011 season. Patient age, the presence of underlying conditions, pneumonia, acute respiratory distress syndrome (ARDS) and the need for ventilation were significantly associated with the severity of influenza A(H1N1)pdm09 infection. Despite limitations essentially because of the heterogeneity of the data reported, this study provides insight into severe influenza cases.

Keywords Europe, influenza A(H1N1)pdm09, risk factors, severity, surveillance.

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Background

The severity of influenza disease is usually estimated retrospectively through observational studies on hospitalisation rates[1] or through mortality data.[2] In addition to these, the surveillance of hospitalised severe laboratory-confirmed influenza cases was implemented for the first time following the emergence of the influenza A(H1N1)pdm09 pandemic virus. In 2010–2011, data reported on a voluntary basis to the European Centre for Disease Prevention and Control (ECDC) were standardised across countries enabling timely pooled data analysis of severe influenza cases across a sample of EU countries, which resulted in a larger sample size of the population assessed. The objective of this study was to describe the demographic, clinical characteristics and vaccination status among hospitalised severe A(H1N1)pdm09 influenza cases.

Methods

During the 2010–2011 season (weeks 40–20), case-based data for hospitalised influenza infections were uploaded weekly on a voluntary basis to The European Surveillance System (TESSy) by Austria, Finland, France, Ireland, Malta, Portugal, Romania, Slovakia and Spain.

The following information was collected on each case for analysis: laboratory confirmation of influenza A(H1N1)pdm09 infection, type of hospitalisation (inpatients admitted to regular care versus patients in ICU) and outcome (non-fatal versus fatal). Patients without all of the above-mentioned data were excluded from further analysis. In addition, demographic data (age and gender), clinical data (underlying conditions, complications and oxygen support) and vaccination status were collected. Patients were categorised into three groups according to the level of severity of disease: group 1 = non-fatal cases admitted to regular inpatient care, group 2 = non-fatal cases admitted to ICU and group 3 = fatal cases. Descriptive statistics, chi-squared tests and regression models for calculating the overall statistical association across the three severity groups ($P < 0{\cdot}05$) and correlation coefficient (R^2) were performed using Stata Statistical Software (Release 12: StataCorp 2011, College Station, TX, USA)

Results

Of the 3292 cases reported, 1021 (31%) were excluded as they did not report outcome (20·3%), type of hospitalisation (4·9%) and/or laboratory confirmation of influenza A(H1N1)pdm09 infection (10·2%). After excluding these

cases, a total of 2271 hospitalised laboratory-confirmed influenza A(H1N1)pdm09 were included in the analysis. The distribution of A(H1N1)pdm09 cases is tabulated in Table 1.

The 2271 cases were divided into three groups: 1056 patients were classified as the least severe (group 1), 860 as ICU non-fatal cases (group 2) and 355 as fatal cases (group 3). Key patient characteristics and their statistical association with severity of infection, defined by group, are displayed in Table 2.

Median patient age was significantly ($P < 0{\cdot}01$) associated with the level of disease severity and was 41, 48 and 53 years respectively. The percentage of patients immunised against the influenza A(H1N1)pdm09 virus, with the mono- or trivalent vaccines available in 2010, was similar across the three groups: 14·5%, 15·3% and 15·7%, respectively. Of 1483 patients for whom information was available, 1075 (72·5%) reported at least one underlying condition and 408 (27·5%) reported no underlying condition. In addition, the prevalence of one or more underlying conditions was significantly associated with the level of severity and increased with increasing severity: 66%, 72·9% and 88·2% in the three groups, respectively. Chronic lung diseases (including asthma), diabetes mellitus, heart diseases and HIV represented 51% of patients with documented underlying conditions ($n = 1483$). In addition, the prevalence of obesity and pregnancy was, respectively, 14·5% and 4·9%. The vast majority of fatal cases (88·2%) occurred in patients with at least one underlying condition ($n = 225$) resulting in a case fatality ratio (CFR) of 20·9%, while the proportion of deaths in patients without underlying conditions ($n = 30$) was 11·8% ($\chi^2 = 38{\cdot}29$, $P < 0{\cdot}001$) resulting in a CFR of 7·4%. Obesity, including morbid obesity (BMI ≥ 40), was significantly associated with the disease severity. Of 215 obese persons, 46 (21·4%) had at least one additional underlying condition. Of 72 pregnant women for whom information on underlying conditions was available, one had an additional underlying condition and survived, while eleven (15·3%) had no additional underlying conditions, yet died in ICU. The prevalence of the main clinical complications, that is, secondary pneumonia and acute respiratory distress syndrome (ARDS), was significantly associated with disease severity. Oxygen ventilation was required in most of the fatal cases and in most of the non-fatal cases admitted to the ICU, but hardly ever in the non-fatal cases admitted to regular care. The majority (77·5%) of deaths occurred in patients aged less than 65 years. Nevertheless, the CFR increased with increasing age and was highly correlated with age ($R^2 = 0{\cdot}98$) ranging from 3·9% in 0 to 4-year-olds up to 20·8% in ≥65-year-olds (Figure 1).

Table 1. Distribution of A(H1N1)pdm09 cases across countries

Countries	Number of cases	%
Austria	371	16·3
Spain	854	37·6
Finland	58	2·6
France	441	19·4
Ireland	105	4·6
Malta	48	2·1
Portugal	284	12·5
Romania	83	3·7
Slovakia	27	1·2
Total	2271	100

Discussion

Our study showed that age, underlying medical conditions, clinical complications and the need for ventilation were significantly associated with the severity of the influenza A(H1N1)pdm09 infection. Comparable results were reported by other studies with a similar focus on hospitalised influenza A(H1N1)pdm09 cases, even though their frameworks and settings differed from ours. Increasing age was significantly associated with the level of severity as confirmed by other studies.[3,4] Similar to seasonal influenza outbreaks, patients with underlying conditions, in particular chronic lung and heart disease, were at increased risk of more severe outcomes.[4–6] Furthermore, obesity, in particular morbid obesity, and pregnancy were also considered as particular risk factors for complications of A(H1N1)pdm09 infection.[5,7–9] As vaccination coverage was unexpectedly not significantly associated with the level of disease severity, further studies about vaccine coverage and effectiveness in severe A(H1N1)pdm09 influenza cases are needed. The low proportion of additional underlying conditions in obese patients and in pregnant women in comparison with other studies,[6,10–13] even during influenza seasons,[14] might be explained by possible under-reporting. Additional reasons might be due to reporting differences between countries that were impossible to evaluate in this study. As observed in other studies,[4,10] the proportion of patients with no underlying condition is noteworthy. Not surprisingly, cases with at least one underlying condition accounted for the vast majority of deaths. The very significant linear increase of mortality with increasing age might be related to a higher proportion of underlying conditions in older patients. Severe pulmonary complications and the need for ventilation increased with the level of severity as also observed in other studies.[4,15]

The added value of this severe influenza surveillance is its EU dimension and the first-ever implementation of surveillance of severe influenza cases where data were

Table 2. Influenza A(H1N1)pdm09 patient characteristics by group and the level of association (chi-squared tests; *P*-value) across the three disease severity groups

Patient Characteristics	Group 1 Non fatal inpatients not in ICU		Group 2 Non fatal patients in ICU		Group 3 Fatal cases		*P*-value
	n/N***	%	*n/N*	%	*n/N*	%	
Age <1 year	66/1056	6·3	21/860	2·4	3/355	0·8	***
Age ≥65 year	186/1056	17·6	104/860	12·1	80/355	22·5	0·8
Male	575/1054	54·6	484/856	56·5	200/354	65·5	0·4
Vaccinated	92/635	14·5	95/619	15·3	33/210	15·7	0·6
More than 1 condition	428/649	66·0	422/579	72·9	225/255	88·2	<0·01
Complications:							<0·01
ARDS	53/711	7·5	351/649	54·1	151/309	48·9	<0·01
Pneumonia	448/699	64·1	291/640	45·5	164/307	53·4	<0·01
Need for ventilation	10/388	2·6	451/535	84·3	171/186	91·9	<0·01

*Observation number.
**Total number of observations in the dataset.
***No *P*-value due to low sample size.

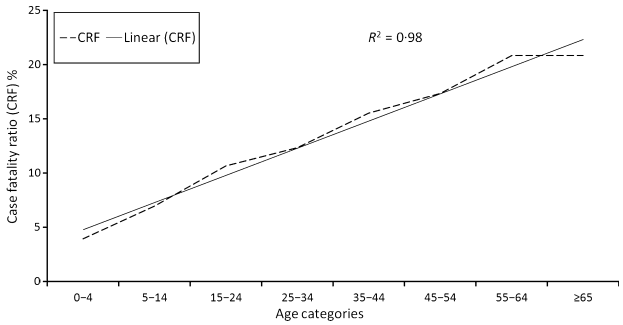

Figure 1. Correlation between case fatality ratio and pre-defined age groups.

uploaded to The European Surveillance System (TESSy) of ECDC in a timely fashion. Also this study provides confirmation to previously conducted observational studies based on surveillance data.

One possible limitation of the study includes, as in all facility-based studies, the representativeness of the data. In most cases, it was impossible to determine the population denominator for the cases reported, as some countries reporting collected data from robust sentinel sites with known denominators, while other used opportunistic samples from hospitals. This limitation prevented the calculation of, for example, disease incidence rates. Also, antiviral prophylaxis, non-pharmaceutical interventions and criteria for hospital admission differed substantially across countries and even over time. Direct comparisons of results from this study with those from other studies carried out during the pandemic season need to be interpreted with caution as the pattern and the outcome of influenza A(H1N1)pdm09 infection may be different.

In conclusion, despite the limitations, our key results provide insight into the main characteristics of hospitalised severe A(H1N1)pdm09 influenza cases and are consistent with those from other studies. These results highlight the necessity for the standardisation of the surveillance of severe influenza at EU level to support member states in developing and maintaining suitable surveillance systems.

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