

Impact of the 2009/2010 influenza A (H1N1) pandemic on trends in influenza hospitalization, diagnostic testing, and treatment

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Analysis of a US hospitalization database demonstrated that more influenza patients were hospitalized and the age distribution of hospitalizations was younger during the 2009 (H1N1) influenza A pandemic compared with the three previous influenza seasons. The duration of hospital stay remained stable in all four seasons. A higher proportion of patients was treated with antivirals ($P < 0.0001$), comprised almost entirely of neuraminidase

inhibitors, and the proportion was highest in those with influenza confirmed by diagnostic testing ($P < 0.0001$). Approximately one-third remained untreated. Young children had the lowest rate of neuraminidase-inhibitor treatment during the 2009 pandemic ($P < 0.05$).

Keywords Antivirals, hospitalization, influenza.

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Introduction

The 2009 (H1N1) influenza A pandemic created a public health emergency in the USA.¹ Rates of hospitalization, admission to ICUs, and invasive life support seemed higher than observed for seasonal influenza.^{2,3} By mid-December, an estimated 55 million were infected and 246 000 were hospitalized in the USA;⁴ a modeling approach used in another study provided even higher estimates.⁵ The Centers for Disease Control and Prevention and the World Health Organization recommended early treatment with antivirals in patients hospitalized with 2009 (H1N1) influenza A.^{6,7} In uncontrolled cohort studies in hospitalized influenza patients, early use of antivirals, particularly neuraminidase inhibitors (NAIs), was associated with improved survival and shorter hospital stays.^{8,9} We used a large electronic database to evaluate the impact of the 2009 (H1N1) pandemic on the diagnosis of, hospitalization of, and treatment for influenza in the USA compared with previous seasons.

Study design

The SDI database used for this study contained standardized, patient-level, anonymized healthcare encounter records for all patients admitted to a large sample (approx-

imately 20%) of non-government-funded hospitals in the USA. In 2009, the database included patients from hospitals in all 50 states that were urban (85%) and medium- to large-sized (100–500 beds) (72%); 36% were teaching hospitals. Records from October 2006 through March 2010 were included in the study; they were representative of the population with regard to age, gender, and regional distribution and included all payers (i.e., Medicare/Medicaid, third-party payer claims, and cash). De-identified HIPAA-compliant patient information was made available in the database within 2–4 weeks of discharge.

We selected records containing a discharge diagnosis of influenza (ICD-9 codes 487–488) for patients discharged during October 2006–March 2010. We compared the influenza seasons of 2006–2007, 2007–2008, and 2008–2009 (October–April) to two waves of the 2009 (H1N1) pandemic (May–July 2009 and August 2009–March 2010) for the number of hospitalized influenza cases, age of patients, use of diagnostic tests for influenza [current procedural terminology (CPT) codes for rapid antigen test, polymerase chain reaction test, immunofluorescence, culture, or antibodies], antiviral treatments, and duration of hospital stay.

In the population of patients who were hospitalized, we compared the proportions by age group, use of diagnostic testing, and use of antiviral treatment between seasons or

age groups by a two-sample test for equality of proportions with continuity correction. The duration of hospital stay was compared between seasons by Wilcoxon, Log-Rank, and Log Likelihood tests.

Results

The characteristics of hospitalized patients with influenza diagnosis (total = 37 965) in the SDI database over time are summarized in Table 1. The 2009 (H1N1) influenza A pandemic was unique in commencing in the late spring, having a longer duration, and demonstrating two distinct waves; the number of hospitalized influenza cases was several times larger than that in previous influenza seasons.

Patients in the 2009–2010 pandemic waves had a different age distribution than patients seen in the three preceding seasons (2006–2007: $P = 0.0003$; 2007–2008: $P < 0.0001$; 2008–2009: $P < 0.0001$). A higher proportion of patients in the 2009–2010 pandemic waves were in the 19–64 age group than in the three preceding seasons (2009–2010: 50% versus 2006–2007: 27%, 2007–2008: 31%, 2008–2009: 30%) and fewer were ≥ 65 years old (2009–2010: 12% versus 2006–2007: 24%, 2007–2008: 40%, 2008–2009: 24%). The duration of hospital stay was similar across influenza periods from 2006 to 2010 ($P > 0.05$) with 10–12% of stays ≥ 10 days (Table 1).

The proportion of hospitalized patients that received antiviral therapy increased from 34% in the 2006–2007

season to 70% during the second wave of the 2009 (H1N1) pandemic (Table 1, $P < 0.0001$). Antiviral therapy was comprised almost entirely of NAIs. During the two pandemic waves in 2009/2010, 7061 (33%) of the 21 212 hospitalized influenza patients received no antiviral treatment. Of the subset of influenza patients with a diagnostic test recorded, 71% were treated with antivirals compared to 58% of patients without a test, indicating that tested patients were 1.8 times more likely than untested to receive antiviral treatment (OR 1.8; 95% CI, 1.67–1.88; $P < 0.0001$). The proportion of hospitalized influenza patients that had a diagnostic test to confirm influenza remained fairly constant during the study period.

During the three previous influenza seasons, the rate of treatment with antivirals was greater for adults than for children (Figure 1). From 2006 to 2009, a higher proportion of adults ≥ 19 years of age hospitalized with seasonal influenza (52%) were treated with antivirals compared with children (15%, $P < 0.001$). This age-related difference disappeared during the pandemic except for those patients 0–5 years (56%) compared with ≥ 6 years (70%, $P = 0.046$).

Discussion

Results from this study of recent influenza trends in a 20% sample of US hospitals show that substantially more patients were hospitalized with influenza during the 2009 (H1N1) influenza A pandemic than in three previous influ-

Table 1. Characteristics of hospitalized influenza patients from the SDI database by season

Description	October 2006– April 2007	October 2007– April 2008	October 2008– April 2009	May 2009– July 2009	August 2009– March 2010
Total diagnosed with influenza	3453	9162	4138	3545	17 667
Age group, <i>n</i> (%)					
0–5 years	1275 (37)	2110 (23)	1592 (38)	971 (27)	4076 (23)
6–18 years	386 (11)	513 (6)	529 (13)	590 (17)	2428 (14)
19–64 years	948 (27)	2832 (31)	1250 (30)	1584 (45)	9079 (51)
≥ 65 years	844 (24)	3707 (40)	767 (19)	400 (11)	2084 (12)
Duration of hospital stay, <i>n</i> (%)					
1–2 days	1496 (43)	3295 (36)	1786 (43)	1448 (41)	6999 (40)
3–5 days	1178 (34)	3449 (38)	1406 (34)	1170 (33)	6125 (35)
6–9 days	431 (12)	1435 (16)	542 (13)	492 (14)	2433 (14)
≥ 10 days	348 (10)	983 (11)	404 (10)	435 (12)	2110 (12)
Diagnostic test, <i>n</i> (%)	2182 (63)	5780 (63)	2640 (64)	2549 (72)	11 247 (64)
Antiviral therapy, <i>n</i> (%)*					
Adamantanes	59 (2)	114 (2)	338 (8)	134 (4)	215 (1)
NAIs	1129 (33)	3878 (42)	1172 (28)	1838 (52)	12285 (70)
Peramivir	0	2	0	0	10
No antivirals	2278 (66)	5208 (57)	2886 (70)	1704 (48)	5357 (30)

NAI, neuraminidase inhibitor.

*Patients may have used more than one antiviral medication.

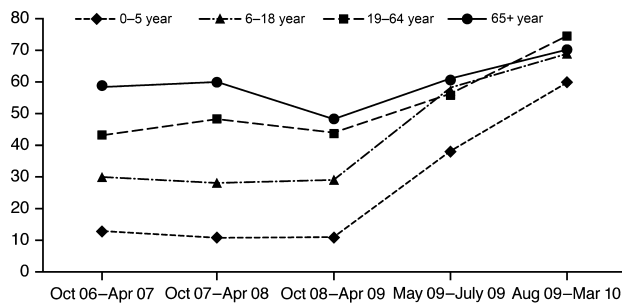


Figure 1. The proportion of hospitalized patients in each age group who were treated with antivirals by influenza season.

enza seasons. This likely reflects the lack of pre-existing immunity to the novel H1N1 strain in persons under 65 years and its tropism to the lower respiratory tract.¹⁰ The age distribution of hospitalizations was younger than that of previous seasons, consistent with the “signature age shift” typically experienced with pandemic influenza.¹¹ These data are consistent with other reports from studies of 2009 pandemic influenza patients in the USA.^{12–14}

We found that treatment with antivirals, particularly NAIs, was more prevalent during the 2009 (H1N1) pandemic than in pre-pandemic influenza seasons, possibly due to awareness of the pandemic, concerns about disease severity, and available guidelines that stressed early treatment of hospitalized patients.⁶ In a case study of hospitalized US patients in the first wave of the pandemic, Jain *et al.*² reported that 75% of approximately 200 patients received antiviral treatment. We studied considerably more patients and found lower rates; 52% and 70% of patients in the first and second waves of the pandemic, respectively, were treated with antivirals; of these, only 7% and 2%, respectively, were treated with adamantanes. The low use of adamantanes may reflect early knowledge of the high rate of adamantane resistance and oseltamivir sensitivity of the 2009 pandemic H1N1 viruses and public health authority guidance.¹³ As expected, absence of diagnostic influenza testing was associated with a lower rate of antiviral treatment.

Our data revealed that in previous seasons, older hospitalized patients were more likely to be treated with antivirals than younger patients, perhaps because of awareness of their higher mortality rates. In the 2009 (H1N1) pandemic, however, the proportion of patients who were treated rose in every age group so that >65% of patients in each of the 6–18 years, 19–64 years, and ≥65 years age groups were treated with antivirals.

The advantages of this electronic database include the timeliness of available data (lag period of only 1–2 months) and access to a large number of records for patients hospitalized with pandemic influenza. However, the study was limited by our use of ICD-9 and influenza CPT codes to

identify patients and the lack of information about the patients’ clinical course, mortality, detailed viral testing, and treatment prior to admission. Also, we did not have access to data on the delay from start of symptoms, diagnosis, and hospitalization to start of treatment, a key limitation given recent reports of the benefits of early oseltamivir treatment.¹⁵ In addition, the reasons for lack of antiviral treatment are not known.

Conclusions

Significantly higher numbers of influenza patients were hospitalized during the 2009 (H1N1) influenza A pandemic and a higher proportion were treated with NAIs during their stay. Despite the increase in treatment for pandemic influenza, many hospitalized patients, especially young children, remained untreated, a potential missed opportunity and contrary to current public health guidelines.⁶ Understanding the reasons for lack of treatment with NAIs is deserving of further study.

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