

Hospital-acquired influenza in an Australian sentinel surveillance system

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Nosocomial influenza has been associated with significant morbidity, mortality and cost due to increased length of stay. It is likely to be under-recognised because of rapid turnover of patients and delays in diagnosis. Most previous reports of nosocomial influenza have involved known case clusters.¹ We aimed to review cases of nosocomial influenza detected in a hospital-based surveillance program.

Methods

The Influenza Complications Alert Network (FluCAN) is a sentinel surveillance system that prospectively collects data on adult patients hospitalised with confirmed influenza.² In 2010, this system involved 15 hospitals in all Australian jurisdictions and, in 2011, eight hospitals in Victoria, the Australian Capital Territory, South Australia and Western Australia. Surveillance was performed between April and November of each year.

Influenza was diagnosed using nucleic-acid detection from respiratory samples. Testing was performed at the discretion of treating clinicians but was encouraged for influenza-like illnesses because of infection prevention considerations. Seasonal influenza subtypes were not recorded, but other surveillance systems suggest that pandemic (H1N1) 2009 influenza was the major circulating strain in 2010 and 2011.³ Patients were identified by surveillance of laboratory testing logs. A nosocomial case was defined as polymerase chain reaction-confirmed influenza where the onset of symptoms was more than 2 days after the patient's admission or, if this was not known, where the date of the positive test was more than 7 days after admission.

Continuous measures were compared using the Mann–Whitney *U*

Abstract

Objective: To review cases of nosocomial influenza and compare the epidemiology, clinical characteristics and outcomes with community-acquired cases.

Design, setting and participants: Prospective case series of adults hospitalised with influenza during April – November of 2010 and 2011 using a hospital-based sentinel surveillance system. A nosocomial case was defined as polymerase chain reaction-confirmed influenza where symptom onset was more than 2 days after admission or, if this was not known, where the date of the positive test was more than 7 days after admission.

Main outcome measures: Demographic, clinical and outcome measures for patients with nosocomial influenza compared with patients admitted with community-acquired influenza.

Results: In 2010–2011, 598 cases of influenza were detected, of which 26 (4.3%) were nosocomial. All patients with nosocomial influenza had chronic comorbidities, compared with 71.7% of patients (410/572) with community-acquired influenza ($P = 0.001$). Similar proportions of community-acquired (32.5%) and nosocomial (36.4%) cases occurred in patients vaccinated in the current season. Clinical findings at time of enrolment did not differ between the two groups, with similar rates of fever, cough, chest pain and dyspnoea. Compared with community-acquired cases, a higher proportion of patients with nosocomial influenza received neuraminidase inhibitors within 2 days of symptom onset (38.5% v 15.9%; $P = 0.003$). Admission to intensive care took place in 21.3% and 23.1% of community-acquired and nosocomial cases, respectively. One death from nosocomial influenza occurred in a patient with end-stage respiratory disease.

Conclusions: Nosocomial influenza is uncommon but may be associated with severe disease. It may be partially preventable as patients frequently have comorbidities for which influenza vaccination is recommended. Patients, particularly those at high risk of complications, and their contacts (including health care workers) should be vaccinated to prevent severe disease.

test, and categorical variables with the χ^2 test or Fisher exact test as appropriate. We calculated crude (unadjusted) odds ratios (ORs) for characteristics of patients with nosocomial and community-acquired influenza. All statistical analysis was performed using Stata 12.1 (StataCorp). Ethics approval for the study was obtained from all sites and the Australian National University.

Results

Diagnosis of influenza

Of 598 patients diagnosed with confirmed influenza in the 2010 and 2011 surveillance periods, 26 (4.3%) had nosocomial influenza (Box 1). Cases

were seen at multiple hospitals and were coincident with the presentation of community-acquired cases (data not shown). Compared with community-acquired cases, nosocomial cases were diagnosed sooner after onset of symptoms (Box 2). Symptom onset in the nosocomial group occurred a median of 12.5 days after admission.

Demographic characteristics and comorbidities

All patients with nosocomial influenza had chronic comorbidities, compared with 71.7% of community-acquired cases ($P = 0.001$) (Box 1). Patients with nosocomial influenza were significantly more likely to be immunosuppressed or have an underlying malignancy. Of the 22

nosocomial cases where vaccination status was known, eight patients (36.4%) had been vaccinated against influenza in the current season.

Clinical characteristics and initial treatment

Clinical findings at time of enrolment did not differ between the two groups, with similar rates of fever, cough, chest pain and dyspnoea (data not shown). Similar proportions of patients in both groups were treated with neuraminidase inhibitors. Treatment was initiated earlier in the nosocomial group, and a significantly higher proportion of this group received treatment within 2 days of onset of symptoms (Box 2).

Course of illness

The hospital stay included an admission to the intensive care unit (ICU) for 21.3% and 23.1% of patients with community-acquired and nosocomial influenza, respectively (Box 2). Of the six patients with nosocomial influenza who were cared for in the ICU, three were diagnosed before admission to the ICU.

Mortality

One patient, a man aged in his 40s with end-stage respiratory disease and renal disease requiring dialysis, died from nosocomial influenza. He had not been vaccinated against influenza. Influenza A (H3N2) was diagnosed on Day 18 of his admission, and he was treated with a 5-day course of oseltamivir. The patient died 2 weeks later from worsening respiratory failure.

Discussion

We found that nosocomial influenza was uncommon but may be severe. Our finding that 4.3% of hospitalised influenza patients had nosocomial influenza is similar to that from an observational cohort study in the United Kingdom in 2009–2010, which detected 30 nosocomial cases (2.0%) in 1520 hospitalised patients with influenza at 75 hospitals.⁴ The low numbers and high severity of illness may suggest underdiagnosis of mild cases, patients presenting after discharge, or the susceptibility of hospitalised patients with significant

1 Demographic characteristics and comorbidities of patients with community-acquired or nosocomial influenza

Variable	Community-acquired influenza	Nosocomial influenza	Odds ratio (95% CI)
Number of patients	572	26	
Male	273 (47.7%)	14 (53.8%)	1.3 (0.5–3.1)
Median age (range)	44 (0–93)	52 (26–89)	—*
Indigenous	24 (4.2%)	1 (3.8%)	0.9 (0.0–6.1)
Nursing home resident	11 (1.9%)	0	nd (0–7.7)
Pregnant	32 (5.6%)	1 (3.8%)	0.7 (0.0–4.4)
Smoker	120 (21.0%)	6 (23.1%)	1.1 (0.4–3.0)
Any chronic comorbidity	410 (71.7%)	26 (100.0%)	nd (2.7–nd)
Chronic obstructive pulmonary disease	17 (3.0%)	1 (3.8%)	1.3 (0.0–9.0)
Asthma	63 (11.0%)	2 (7.7%)	0.7 (0.1–2.8)
Diabetes	84 (14.7%)	6 (23.1%)	1.7 (0.6–4.7)
Immunosuppression	114 (19.9%)	13 (50.0%)	4.0 (1.7–9.7)
Malignancy	33 (5.8%)	4 (15.4%)	3.0 (0.7–9.5)
Cardiac disease	77 (13.5%)	2 (7.7%)	0.5 (0.1–2.2)
Neurological disease	51 (8.9%)	1 (3.8%)	0.4 (0.0–2.6)
Renal disease	43 (7.5%)	4 (15.4%)	2.2 (0.5–7.0)
Vaccinated in current season	101/311 (32.5%)	8/22 (36.4%)	1.2 (0.4–3.1)

nd = not defined. * $P = 0.41$.

2 Diagnosis and treatment of community-acquired or nosocomial influenza

Variable	Community-acquired influenza*	Nosocomial influenza†	Odds ratio (95% CI)	P
Median days to diagnosis from onset of symptoms (range)	4 (0–41)	1.5 (0–8)		< 0.001
Delay to testing ≤ 2 days	173 (30.2%)	17 (65.4%)	4.4 (1.8–11.3)	< 0.001
Median days hospitalised before onset of influenza symptoms (range)	na	12.5 (3–64)		—
Influenza type				
Influenza A	514 (89.9%)	24 (92.3%)	1.4 (0.3–12.1)	0.51
Influenza B	58 (10.1%)	2 (7.7%)	0.7 (0.1–3.1)	0.69
Treated with oseltamivir or zanamivir	337/529 (63.7%)	16/25 (64.0%)	1.0 (0.4–2.7)	0.93
Median days to treatment from symptom onset (IQR)	4 (2–6)	2 (2–3)		0.004
Delay to treatment ≤ 2 days	91 (15.9%)	10 (38.5%)	3.3 (1.3–8.0)	0.003
Treated with antibiotics	249/271 (91.9%)	7/11 (63.6%)	0.2 (0.0–0.8)	0.002
Admitted to intensive care unit	122 (21.3%)	6 (23.1%)	1.1 (0.4–2.9)	0.91
Mechanical ventilation	61/122 (50.0%)	4/6 (66.7%)	2.0 (0.3–22.8)	0.52
Vasopressor support	65/122 (53.3%)	0/6		0.06
Died	17 (3.0%)	1 (3.8%)	1.3 (0.0–9.0)	0.56
Median days hospitalised before diagnosis (IQR)	na	15.5 (7–32)		—
Median days hospitalised after diagnosis (IQR)	4.0 (2–7)	27.5 (3–35)		< 0.001

na = not applicable. IQR = interquartile range. * Denominator is 572 unless otherwise specified. † Denominator is 26 unless otherwise specified.

comorbidities, particularly malignancy and immunosuppression, reflected in the nosocomial cases reported here.^{2,5}

Poor outcomes have been described for nosocomial influenza, particularly in neonates and in patients who are immunosuppressed.⁴ In our study, the proportion of patients requiring ICU admission

was similar in the nosocomial and community-acquired influenza groups. This differs from the UK cohort,⁴ where more than half the patients with nosocomial influenza required intensive care support. Mortality in nosocomial cases was also low in our study, with only one death noted, while mortality as high as 26.7% was reported in the UK study.⁴

Compared with community-acquired influenza cases, we noted a significantly longer length of stay for patients with nosocomial influenza, but there are likely numerous factors confounding this observation. Nosocomial influenza has previously been associated with an increased hospitalisation duration of 8 days, as well as increased use of diagnostics and treatment.⁵

Strategies to reduce nosocomial transmission of influenza include vaccination of patients before the winter season, vaccination of contacts including health care workers and visitors, more effective barrier precautions including improving hand hygiene compliance, and encouraging staff to stay away from work when unwell. Although influenza vaccination is publicly funded for older people and those with chronic comorbidities, protection is incomplete. We found that vaccination failed in a third of patients and two-thirds were not vaccinated, consistent with studies estimating vaccine effectiveness against medically attended influenza⁶ and hospitalisation with pandemic (H1N1) 2009 influenza at 49%–59%.⁷ Interventions to reduce transmission from infected contacts through barrier precautions and advice not to work or visit when unwell are hampered by infectivity before symptoms appear or by minimally symptomatic infection. Prophylactic antivirals are probably only feasible to contain outbreaks in closed facilities. Less than half of the

patients with nosocomial influenza in our study received treatment with antivirals within 48 hours of symptom onset. This may reflect delays in diagnosis and the lack of efficacy of antivirals after 48 hours. This proportion is lower than in the UK cohort, where 57% of 21 patients received antivirals within 48 hours of onset of symptoms.⁴

The proportion of health care workers known to be vaccinated in Australian hospitals has been reported at around 40%.⁸ Although two cluster-randomised trials found that mortality was lower in long-term care facilities where vaccination was actively promoted, the conclusions have been criticised because of methodological concerns.⁹ The results appeared to be internally inconsistent, with a large mortality benefit despite a lack of detection of significant influenza disease. There has been recent interest in making influenza vaccination a mandatory condition of working with patients, and this policy has been implemented with some success in the United States.¹⁰ It is not clear whether the patients identified in our study acquired infection from health care workers, from other infected patients or from visitors.

Our results suggest that a small proportion of influenza cases detected in hospitalised patients are acquired during the hospital stay, and that this may be associated with severe disease in a significant proportion of these patients. The overwhelming majority of nosocomial influenza occurs in

patients with pre-existing medical illness that places them at high risk of complications.

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