H1N1 Influenza A (Swine Flu) Alert Center

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H1N1 Critical Illness Mostly Affects Young Patients and Is Often Fatal

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Authors and Disclosures

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October 12, 2009 — H1N1 critical illness mostly affects young patients and is often fatal, according to the results of a Canadian and Mexican study and an editorial published online October 12 in the *Journal of the American Medical Association* (*JAMA*).

"Between March and July 2009, the largest number of confirmed cases of 2009 influenza A(H1N1) infection occurred in North America," write Anand Kumar, MD, from the Health Sciences Centre and St. Boniface Hospital in Winnipeg, Manitoba, Canada, and colleagues with the Canadian Critical Care Trials Group H1N1 Collaborative.

The goal of this prospective observational study was to evaluate clinical characteristics, treatment, and outcomes of critically ill patients who had 2009 influenza A (H1N1) infection in Canada. Between April 16 and August 12, 2009, 168 critically ill patients with 2009 influenza A (H1N1) infection in 38 adult and pediatric intensive care units (ICUs) in Canada were followed up for 28-day and 90-day mortality. Secondary study endpoints included frequency and duration of mechanical ventilation and duration of ICU stay.

Of 215 patients with critical illness, 162 had confirmed, 6 had probable, and 47 had suspected community-acquired 2009 influenza A (H1N1) infection. Mean age was 32.3 ± 21.4 years in the 168 patients with confirmed or probable 2009 influenza A (H1N1); 113 patients (67.3%) were women and girls, 50 patients (29.8%) were children, and 43 patients (25.6%) were aboriginal Canadians.

Among critically ill patients, overall 28-day mortality was 14.3% (95% confidence interval [CI], 9.5% – 20.7%), and shock and nonpulmonary acute organ dysfunction were common (sequential organ failure assessment mean score 6.8 ± 3.6 on day 1). At 90 days, overall mortality was 17.3% (95% CI, 12.0% – 24.0%; n = 29).

At ICU admission, all patients were severely hypoxemic (mean ratio of partial pressure of oxygen in arterial blood [PaO_2] to fraction of inspired oxygen [FIO_2] of 147 ± 128 mm Hg). Median time from symptom onset to hospital admission was 4 days (interquartile range [IQR], 2 – 7 days) and from hospitalization to ICU admission was 1 day (IQR, 0 – 2 days).

Most critically ill patients received neuraminidase inhibitors (n = 152 [90.5%]) and mechanical ventilation (n = 136 [81.0%]). Median duration of ventilation was 12 days (IQR, 6 – 20 days) and of ICU stay was 12 days (IQR, 5 – 20 days). Some patients also required lung rescue therapies, including neuromuscular blockade in 28% of patients, inhaled nitric oxide in 13.7%, high-frequency oscillatory ventilation in 11.9%, extracorporeal membrane oxygenation in 4.2%, and prone positioning ventilation in 3.0%.

"Critical illness due to 2009 influenza A(H1N1) in Canada occurred rapidly after hospital admission, often in young adults, and was associated with severe hypoxemia, multisystem organ failure, a requirement for prolonged mechanical ventilation, and the frequent use of rescue therapies," the study authors write. "Our data suggest that severe disease and mortality in the current outbreak is concentrated in relatively healthy adolescents and adults between the ages of 10 and 60 years, a pattern reminiscent of the W-shaped curve previously seen only during the 1918 H1N1 Spanish pandemic."

Limitations of this study include focus on severe disease requiring ICU admission, possible late deaths occurring after the observation period, and possible overrepresentation or underrepresentation of certain comorbidities and clinical features.

"We have demonstrated that 2009 influenza A(H1N1) infection–related critical illness predominantly affects young patients with few major comorbidities and is associated with severe hypoxemic respiratory failure, often requiring prolonged mechanical ventilation and rescue therapies," the study authors conclude. "With such therapy, we found that most patients can be supported through their critical illness."

Mexican Study

The goal of the second observational study was to describe baseline characteristics, treatment, and outcomes of critically ill patients with confirmed, probable, or suspected 2009 influenza A (H1N1) in 6 Mexico hospitals. Between March 24 and June 1, 2009, the investigators collected demographic data, symptoms, comorbid conditions, illness progression, treatments, and clinical outcomes from 58 critically ill patients

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with 2009 influenza A (H1N1). The main study endpoint was mortality, and secondary endpoints were rate of 2009 influenza A (H1N1)–related critical illness and mechanical ventilation and length of stay in the hospital and ICU.

Of 899 patients hospitalized with confirmed, probable, or suspected 2009 influenza (A) H1N1, 58 (6.5%) were critically ill. All presented with fever, and 57 of 58 presented with respiratory symptoms; median age was 44.0 years (range, 10 – 83 years). Although comorbid respiratory disorders occurred in few patients, 21 patients (36%) were obese. Median time from hospital to ICU admission was 1 day (IQR, 0 – 3 days). Mechanical ventilation for severe acute respiratory distress syndrome and refractory hypoxemia was needed in 56 of 58 patients. Median day 1 ratio of PaO_2 to FIO_2 was 83 mm Hg (IQR, 59 – 145).

Mortality by 60 days was 41.4% (24 deaths; 95% CI, 28.9% – 55.0%), with 19 deaths occurring within the first 2 weeks. Factors associated with mortality were greater initial severity of illness, worse hypoxemia, higher creatine kinase levels, higher creatinine levels, and ongoing organ dysfunction. Neuraminidase inhibitor treatment (vs no treatment) was associated with better survival, after adjustment for a reduced opportunity to receive neuraminidase inhibitors among patients dying early (odds ratio, 7.4; 95% CI, 1.8 – 31.0).

"Critical illness from 2009 influenza A(H1N1) in Mexico occurred in young individuals, was associated with severe acute respiratory distress syndrome and shock, and had a high case-fatality rate," write Guillermo Domínguez-Cherit, MD, from Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubirán," Mexico City, and colleagues. "Fever and respiratory symptoms were harbingers of disease in almost all cases. There was a relatively long period of illness prior to presentation to the hospital, followed by a short period of acute and severe respiratory deterioration."

Study limitations include relatively early examination of the epidemiology of a severe infectious disease with possible overestimation of case-fatality rate.

"Early recognition of disease by the consistent symptoms of fever and a respiratory illness during times of outbreak, with prompt medical attention including neuraminidase inhibitors and aggressive support of oxygenation failure and subsequent organ dysfunction, may provide opportunities to mitigate the progression of illness and mortality observed in Mexico," the study authors conclude.

In an accompanying editorial, Douglas B. White, MD, MAS, and *JAMA* Contributing Editor Derek C. Angus, MD, MPH, from the University of Pittsburgh School of Medicine in Pennsylvania, note that many US hospitals may be inadequately staffed to provide treatment of the most seriously ill patients with 2009 influenza A (H1N1) in a timely fashion.

"Hospitals must develop explicit policies to equitably determine who will and will not receive life support should absolute scarcity occur," Dr. White and Dr. Angus write. "Any deaths from 2009 influenza A(H1N1) will be regrettable, but those that result from insufficient planning and inadequate preparation will be especially tragic."

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