The epidemiology of influenza illness requiring ICU admission in adults has not been well studied. Here we describe the results of surveillance for influenza in adult patients requiring intensive care in Toronto, Canada over 7 influenza seasons by the Toronto Influenza Bacterial Disease Network (TIBDN). TIBDN is a network of hospitals and microbiology laboratories that conduct population-based surveillance for infectious diseases in metropolitan Toronto and Peel region (pop 4 million). Since December 2004, TIBDN has conducted active surveillance for patients with laboratory confirmed influenza (ICU) who require hospital admission (ICU and non-ICU). Each year influenza causes significant morbidity and mortality, particularly among patients at the extremes of age, and those with chronic underlying medical and immunocompromising conditions. The objectives of this analysis were to determine the incidence of influenza requiring ICU admission in our population, to describe the clinical features of infection and to identify risk factors for fatal outcomes.

Methods

Population-based surveillance for laboratory confirmed influenza in adults (>15 yrs) requiring ICU admission (ICU-IC) in Toronto/Peel (pop 4M) was performed from December 2004 to May 2013 (7 influenza seasons). Consecutive patients with a positive direct test (antigen or PCR) for culture were enrolled. From the 2006/7 season to the 2010/11 season, active surveillance for influenza was conducted in 7 of 23 ICUs in the surveillance area. Nasopharyngeal swabs, and some sputum and BAL samples were processed in licensed microbiology labs using ELA, PCR and/or culture. EIA testing was confirmed by culture or PCR whenever possible. From 2007/8 on, all samples were sent to Ontal Public Health for viral typing. Annual audits were conducted to ensure completeness of reporting.

Clinical data, including APACHE II score at ICU admission and Charlson co-morbidity score were collected from all patients. Bacterial co-infections were defined as occurring when a pathogenic bacteria was isolated from blood or a respiratory specimen at the time of presentation. Effective antimicrobials were defined as antimicrobials to which the influenza subtype was likely to be susceptible during that season (e.g. amantadine was effective against H1N1 before 2006). All data were entered, processed and analyzed using SAS version 9.1 and odds ratios were calculated with 95% confidence intervals. Research ethics board approval for the study was obtained from all participating hospitals.

Results

From December 2004 to May 2013, 576 adults (215 yrs) requiring ICU admission for community-acquired influenza were identified: 163 due to 2009 pH1N1 and 413 due to seasonal influenza (157 influenza A/H1N1, 133 influenza A (not subtyped), 11 influenza A/H3N2, 154 A/H1N1 during the 2009/2010 season, and 77 influenza B). The median annual incidence of influenza infection requiring ICU admission was 2.2/100,000 (range 0.38-4.3).

1. Percentage of patients undergoing chronic care and requiring effective antiviral treatment.
2. Percentage of patients undergoing chronic care and requiring mechanical ventilation.
3. Percentage of patients undergoing chronic care and having an ICU mortality.
4. Percentage of patients undergoing chronic care and requiring a ventilator.
5. Percentage of patients undergoing chronic care and requiring a ventilator with mechanical ventilation.
6. Percentage of patients undergoing chronic care and requiring a ventilator with mechanical ventilation and ICU mortality.
7. Percentage of patients undergoing chronic care and requiring a ventilator with mechanical ventilation and ICU mortality and having an ICU mortality.
8. Percentage of patients undergoing chronic care and requiring a ventilator with mechanical ventilation and ICU mortality and having an ICU mortality and requiring effective antiviral treatment.
9. Percentage of patients undergoing chronic care and requiring a ventilator with mechanical ventilation and ICU mortality and having an ICU mortality and requiring effective antiviral treatment and requiring a ventilator.
10. Percentage of patients undergoing chronic care and requiring a ventilator with mechanical ventilation and ICU mortality and having an ICU mortality and requiring effective antiviral treatment and requiring a ventilator and requiring effective antiviral treatment.

In univariate analysis, older patients, nursing home residents and patients with higher Charlson co-morbidity scores, higher APACHE II scores at admission, and bacterial co-infection were significantly more likely to die. In multivariate analysis (see Table 4), older age, residence in long term care, pandemic influenza infection, higher APACHE II score at admission and requirement for mechanical ventilation were associated with death. Although only 16% of patients who received antivirals were treated within 48 hours of symptom onset, treatment with antivirals was associated with survival. We were unable to detect a difference in survival between those who received antivirals early and those who received them later, but our analysis is not adequately powered to rule out such an effect. Similarly, although we were unable to detect an effect of bacterial co-infection on mortality, the point estimate for the odds ratio for mortality was 1.6 (95% CI 0.84-2.5); our analysis may simply be underpowered to detect this effect.

Conclusion

Influenza is an important cause of respiratory illness requiring ICU admission during the winter season in Ontario. Approximately one sixth of influenza cases requiring ICU admission have a laboratory confirmed bacterial co-infection, most commonly due to S. aureus or S. pneumoniae. Age, severity of illness at admission to ICU, residence in long term care and infection with pH1N1 during the pandemic were associated with increased 15 day mortality. Treatment with an effective antiviral was associated with a significant reduction in mortality.

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