A Comparison of Clinical Features and Outcomes of Hospitalization Due to Seasonal and Pandemic Influenza A (H1N1).

Anu Rebbapragada [1,2,3], Steven Drews[4], Karen A. Green[2], Jonathan Gubbay[1,3], Donald E. Low[1,2,3], Allison McGeer[2,3], The Toronto Invasive Bacterial Diseases Network

1. Ontario Agency for Health Protection and Promotion, Public Health Laboratory-Toronto; 2. Mount Sinai Hospital, Toronto; 3. Department of Laboratory Medicine & Pathobiology, University of Toronto; 4. ProvLab Alberta.

ABSTRACT

***Background*: Understanding the severity of illness due to pandemic (H1N1) 2009 (PH1) is important in establishing recommendations for use of vaccine and antivirals. We compare the clinical features and outcomes of severe influenza due to seasonal H1N1 (SH1) and pandemic H1N1 (PH1) Influenza A.**

***Methods:* Since 11/2006, TIBDN has performed population-based surveillance for influenza related hospitalization in Toronto/Peel (pop 4.5M). and subytping for influenza A isolates .**

***Results:* 154 SH1 (122 in 2007/8 season) and 158 PH1 hospitalizations were identified between April to August 2009. PH1 patients were more likely to be male (86, 58% vs. 77, 53%, P=.06), and to have underlying illness predisposing to complications (83, 58% vs 70,48%, P=.02). There was no difference in time from onset of symptoms to hospitalization (median 55h, IQR 30,96). Age distributions were different: for SH1 versus PH1; for SH1: 0-14y 73 cases (48%), 15-44y 29 (19%), 45-64y 15 (10%), >65y 36 (23%); for PH1: 0-14y 52 (33%), 15-44y 43 (28%), 45-64y 33 (21%), and >65y 28 (18%) (P<.001). Compared to SH1, more children hospitalized with PH1 had an underlying illness (Table1, P=.03) and 50% of younger adults, and >75% of older adults had underlying illness. No children required ICU care; one child with PH1 died out of hospital. Adults aged 15-64y with PH1 were more likely to require ICU admission (OR 3.4, 95% CL 1.0,15) than those with SH1. Co-infecting pathogens were identified in 5 SH1 cases (RSV x 2, GAS X 2, *S. pneumoniae* x 1), and 2 PH1 cases (*S. aureus, H.influenzae*).**

Case fatality rates were 6.2% SH1, 2.9% PH1.

***Conclusions:* In hospitalized patients, PH1 infections occurred more commonly in healthy adults aged 14-44; young adults with PH1 were more likely to require ICU admission. Co-infections were uncommon.**

INTRODUCTION

The sudden emergence and rapid community spread of a novel H1N1 swine origin Influenza A strain in April 2009 raised the urgent demand for enhanced surveillance. The World Health Organization announcement that the novel H1N1 strain was a "pandemic" led to widespread concerns about the burden of disease and the capacity of health care systems to cope with a global crisis. Given that annual seasonal influenza outbreaks contribute to high morbidity and mortality, it was critically important to understand the severity of infection associated with the novel H1N1 pandemic strain. Based on the findings from previous Flu seasons, infants are usually more vulnerable to influenza because of the immaturity of their immune systems and lack of previous exposure while, older adults (>65 yrs old) suffer more consequences of influenza such as pneumonia, secondary bacterial infections, exacerbation of asthma and COPD, and cardiac complications) because of their aging immune response and chronic medical conditions. This study aims to examine the associations between age, gender, chronic underlying illness and co-infections and pandemic H1N1 (PH1). In addition we compared the severity of illness between PH1 and seasonal H1N1 (SH1) infection in hospitalized patients.

METHODS

Surveillance Framework: A population-based surveillance study of laboratory-confirmed influenza requiring hospitalization in Metropolitan Toronto and Peel Region, Ontario, Canada, conducted by the Toronto Invasive Bacterial Diseases Network (TIBDN), began on January 1 2005. TIBDN is a network comprising all hospitals and microbiology laboratories serving the population of Metropolitan Toronto and Peel region (pop. 4.5 million in 2006).

All influenza cases were reported to the TIBDN study office where a study number was assigned and initial clinical and microbiology information was collected. All hospitalized cases were forwarded to study nurses to obtain consent, to collect clinical and laboratory data from patient charts and family doctors, and to conduct a short interview with patients. Nasopharyngeal swabs were taken in ER, ICU and medical departments and were processed in site microbiology labs using rapid tests (EIA, DFA) or culturing. Subsequent testing and subtyping was performed at the Toronto Public Health Laboratory at the Ontario Agency for Health Protection and Promotion. We have used Charlson Index as a prognostic indicator for clinical outcomes of adult patients with comorbid conditions since it correlates significantly with mortality, disability, readmission and length of hospital stay. We have looked as well at bacterial co-infections, rate of flu vaccination, use of antibiotics and time of initiation of antivirals.

Figure 1. TIBDN Surveillance Area

Statistical Analysis: All data were entered, processed and analyzed using SAS version 9.1 and odds ratios were calculated with 95% confidence intervals. Research ethics board was obtained from all participating hospitals.

Laboratory Testing Algorithm

Viral RNA Extraction: Nucleic acid was extracted from 200ul of primary specimen by the easyMag NucliSense magnetic extraction method (bioMerieux).

Influenza A detection: Nucleic acid was tested for the presence of the Influenza A matrix gene by the CDC real-time reverse transcriptase polymerase chain reaction (rRT-PCR) protocol (reference method).

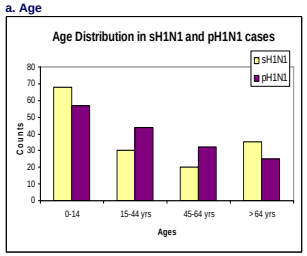
Subtyping: Influenza A-positive specimens were assayed with H1N1 and H3N2 primer sets with rRT-PCR to determine FluA subtype.

Oseltamivir Resistance Detection: Pyrosequencing was performed on FluA H1N1+ isolates to determine whether Histidine 275 on the neuraminidase gene was mutated to Tyrosine (H275Y).

RESULTS

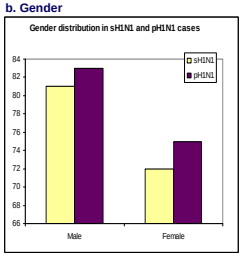
Figure 2. Distribution of Seasonal H1N1 and Pandemic H1N1 Influenza strains in hospitalized cases.

a. Age



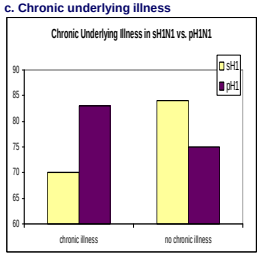
15-44y: 19% vs. 28%
45-64y: 10% vs. 21%,
P<0.001

b. Gender



58% vs. 53%
P=0.06

c. Chronic underlying illness



58% vs. 48%
P=0.02

Table 1. Age Distribution of Seasonal H1N1 and Pandemic H1N1 in chronically ill and ICU cases.

Age Group	Chronic Illness				ICU Admission			
	No. SH1	% SH1	No. PH1	% PH1	No. SH1	% SH1	No. PH1	% PH1
0-15 yrs	17	24%	22	44%	0	**0**	0	**0**
15-44 yrs	11	**42%**	18	**49%**	1	**4%**	8	**21%**
45-64 yrs	11	**92%**	23	**77%**	3	**25%**	12	**30%**
>65yrs	31	**86%**	20	**85%**	9	**25%**	5	**22%**

- **There was a higher proportion of chronic underlying illness in children hospitalized with Pandemic H1N1, compared to Seasonal H1N1 44% vs. 24% (P=0.03).**
- **Underlying illness was found in 50% of younger adults and 77% of older adults with Pandemic H1N1.**
- **No children required ICU care; one child with pH1N1 died out of hospital.**
- **Adults aged 15-64y with Pandemic H1N1 were more likely to require ICU admission (OR 3.4, 95% CL 1.0,15) than those with Seasonal H1N1.**

CONCLUSIONS

- **In hospitalized patients, PH1 infections occurred more commonly in healthy adults aged 14-44.**
- **Young adults with PH1 were more likely to require ICU admission.**