Swiss Medical Weekly
Formerly: Schweizerische Medizinische Wochenschrift
The European Journal of Medical Sciences

Short communication | Published 18 March 2011, doi:10.4414/smw.2011.13177
Cite this as: Swiss Med Wkly. 2011;141:w13177

Clinical features and outcomes of hospitalised adults and children with the 2009 influenza A H1N1 infection at Geneva's University Hospital

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Summary

OBJECTIVE: To describe the clinical features and outcomes of hospitalised cases of the 2009 influenza A H1N1 virus infection at Geneva's University Hospital during the peak of the epidemic.
METHODS: From October 2009 to January 2010, we conducted a four-month prospective case collection of H1N1 laboratory confirmed cases and subsequently reviewed all medical charts of the patients admitted at Geneva's University Hospital.
RESULTS: During the data collection period, 1336 subjects with influenza-like illness were tested for the 2009 H1N1 in Geneva and 451 were positive (34%). A total of 85 patients with confirmed H1N1 were hospitalised (56 adults and 29 children). Patients' median age was 39 years (range 1 month–94years) and the mean hospital length of stay was 12 days. Conditions promoting influenza complications were present in 59% of patients and were mainly asthma, chronic obstructive pulmonary disease (COPD), haematologic disorders and immunosuppressive treatment. The most common reported symptoms were cough, fever, dyspnoea and rhinopharyngitis. Most of the patients (n = 72, 85%) were treated by neuraminidase inhibitors, and 44% (n = 37) received antibiotics for secondary bacterial infection. Fourteen patients (11 adults and 3 children, 16%) developed respiratory failure and were admitted to the intensive care unit (ICU) for respiratory monitoring and/or ventilatory support. The mean ICU length of stay was 11.3 days. The mortality rate was 2.5% among all patients.
CONCLUSIONS: Geneva's experience of the 2009 H1N1 pandemic showed that most of the hospitalised patients were young adults or children. Half of them presented predisposing diseases but only 16% were admitted to the ICU. The mortality rate was low.

Key words: *H1N1; influenza; viruses; hospitalisation; outcome*

Introduction

In April 2009, an influenza A H1N1 of swine origin virus emerged in North America after the seasonal influenza epidemic [1]. Two months later, an international pandemic was declared by the World Health Organization (WHO) [2]. The virus spread quickly to Western Europe including Switzerland where the outbreak peaked in the middle of November 2009 [3]. In February 2010, the Swiss Federal Office of Public Health (OFSP) had identified 13'441 laboratory proven cases of influenza A H1N1 in Switzerland [3]. Among them, 568 (4.2%) were hospitalised. In this group, 268 (47%) belonged to a risk group, 108 (0.8%) were admitted to the intensive care unit (ICU) and 18 (0.13%) died. We aimed to describe the main medical conditions and clinical features associated with hospitalisation and ICU admission due to influenza A H1N1 in our area.

Method

In this observational study and for a four-month period (October 2009 to January 2010), all influenza A H1N1 laboratory confirmed cases in the canton of Geneva were prospectively identified. The influenza A H1N1 diagnosis was confirmed by quantitative reverse transcriptase polymerase chain reaction assay (RT-PCR) on nasopharyngeal specimens.

We subsequently reviewed medical charts of 85 identified cases admitted at Geneva's University Hospital in the department of Internal Medicine and Paediatrics. Clinical characteristics, underlying conditions, respiratory symptoms, and prescribed treatment (antiviral and/or antibiotics) were recorded as well as length of hospital stay, ICU admission and outcomes. Chest radiologic findings were systematically reviewed by a radiologist. The study protocol was approved by the institutional research ethics committee.

Variables are reported as mean ± standard deviation (SD). Comparison between groups was performed using unpaired t tests, chi-square tests or Fischer's exact test when appropriate. The results are presented as odds ratios (OR) with 95% confidence intervals (95%CI). p values <0.05 were considered statistically significant. All statistical analyses were performed using SPSS (version 15.0 for Windows, Chicago, IL, USA).

Results

From October 2009 to January 2010, 1336 subjects with influenza-like symptoms were tested for the influenza A H1N1 at Geneva's Hospital and 451 (34%) were found to be positive. A total of 85 patients with confirmed influenza A H1N1 were admitted to the department of Internal Medicine (n = 56) or Paediatrics (n = 29). The mean hospital length of stay was 12 ± 15.2 days (13.6 ± 16.1 and 7.8 ± 12.6 for adults and paediatric subjects respectively). Patients' main characteristics, underlying conditions, symptoms and treatment are shown in table 1.

A total of 68 patients (80%) were younger than 65 years old with a medium age of 39 years (range 1 month to 94 years) and half of them were male (n = 45, 53%). Most of the patients had typical influenza-like illness including cough (n = 77, 91%), fever (n = 72, 85 %), and/or rhinopharyngitis (n = 40, 47%). Although 7 out of 10 patients reported dyspnoea, abnormalities in chest radiography suggestive of pneumonia were detected in only 32% of all patients. In patients without radiologic pulmonary infiltrates, dyspnoea was mainly explained by severe bronchitis, bronchospasm or concomitant cardiac failure, especially in older patients. Of note, gastrointestinal symptoms were reported in almost one out of five patients (n = 19, 22%).

Four patients (5%) had been recently vaccinated against influenza A H1N1 2009. One girl (aged 10) suffered from sickle cell anaemia and was vaccinated against seasonal influenza as well. Two patients suffered from chronic pulmonary disease (COPD and pulmonary malformation) and one had no underlying condition. The mean delay between the vaccination and hospital admission was 18.3 ± 14.4 days.

The most common pre-existing risks factors for influenza complications identified in hospitalised cases were chronic pulmonary disorders (including asthma) (n = 28, 32%), lymphohematopoeitic cancers and other haematological disorders (n = 9, 11%) (table1). The proportion of haematological disorders was similar in children but pulmonary disorders were less frequently encountered than in adults. Furthermore, a few children suffered from rare diseases such as malformations (cardiac, pulmonary malformation or biliary atresia), Crohn disease or leucinosis.

Eleven cases (13%) were considered to have been acquired nosocomially. These patients developed typical influenza symptoms during their hospital stay after a median duration stay of 13 days (range 2 to 117 days). The patients were either young children (mean age 4.7 ± 6.1 years) or old people (mean age 71.3 ± 10.8 years). Among these 11 cases, risk factors for influenza complications were immunosuppression for 4 patients (leukemia, corticosteroid or other immunosuppressive treatment), hepatic failure due to biliary atresia, chronic renal failure, and a recent heart surgery for 3 other patients. One patient among the 11 (9%) developed an acute respiratory distress syndrome and required mechanical ventilation in the ICU. She was under steroids for a zoster.

Most patients were treated by neuraminidase inhibitors (n = 72, 85%). A total of 96% of adults and 62% of children received oral oseltamivir (Tamiflu®). Most of the time, antiviral medication was started at admission within 3.6 ± 2.5 days after symptoms onset. This delay remains stable when nosocomial cases were excluded (3.7 ± 2.6 days). Compared to the non-ICU patients, ICU patients experienced a longer but not significant delay (3.4 ± 2.6 days and 4.5 ± 2.4 days, respectively (p = 0.85)). Six patients (7%) received intra-venous or inhaled zanamivir combined with oseltamivir, because of the severity of their illness and five of them were admitted to the ICU whereas one was a haematopoietic stem cell recipient. One patient admitted to the ICU had a resistant oseltamivir strain. Almost half of the patients (44%) received antibiotics to treat a lower respiratory tract bacterial infection based on clinical and radiological findings with 73% of them showing pulmonary infiltrate on chest radiography.

The large majority of patients (84%) had a favourable outcome without severe complications requiring ICU admission. Non-ICU patients' mean length of stay was nevertheless 7 ± 6.4 days, which might be explained by the longer need for oxygen in case of pneumonia, the presence of acute bronchospasm (with patients suffering of asthma or COPD), a poor general state, and other co-morbidities, such as renal failure or uncontrolled diabetes mellitus.

Severe cardio-pulmonary complications attributed entirely or in part to influenza A H1N1 occurred in 14 patients (11 adults and 3 children, 16%) who were admitted in ICU. ICU patients' characteristics are also detailed in table 1.

Among these patients, 10 patients (71%) received ventilatory support with non-invasive ventilation (NIV). Seven patients (7/14, 50%) eventually required mechanical ventilation for acute respiratory distress syndrome (ARDS) in six cases and a cardiogenic shock presumably due to an influenza A H1N1 related myocarditis in one case. Six of these 7 patients underwent bronchoscopy with a broncholoalveolar lavage (BAL). For all of them, RT-PCR for influenza A H1N1 RNA detection was positive. These patients underwent further serial virologic testing (BAL, bronchial aspirations or naso-pharyngeal swabs), because of a prolonged viral shedding, with a median duration of 15.5 days. A total of 13 of the 14 patients (93%) were under antibiotic therapy at their admission to the ICU and in 6 cases (43%), a bacteria was identified (mainly Gram-negative bacterias). Ra-

diologic findings showed ground-glass and alveolar opacities in 5 patients (36%), ground-glass infiltrates in 3 patients (21%) and isolated alveolar condensations in 2 (14%). These radiologic images can be features of a viral and/or a bacterial pneumonia. Four patients (29%) did not have any radiologic findings.

The mean length of ICU stay was 11.3 ± 6.4 days. In univariate analysis, factors associated with admission to the ICU for respiratory failure, were presence of dyspnoea at diagnosis (OR 8.47, 95% CI 1.05–68.36) (p = 0.03) and an active haematologic disorder such as multiple myeloma (n = 2), or sickle cell anaemia (n = 2) (OR 4.33 95% CI 1.04–18.1) (p = 0.05).

We documented 2 deaths (2.5%) following ARDS: one 39 year old woman suffering from sickle cell anaemia with important lung fibrosis and pulmonary shunts, and one 49 year old haematopoietic stem cell recipient. No autopsy was done.

Discussion

The outbreak of influenza A H1N1 peaked in November 2009 in Geneva. During these first 3 months, patients hospitalised were mainly young adults and children which is consistent with similar studies throughout the world [4, 6, 7]. This observation may be related to younger people who have a higher likelihood to be exposed to influenza in the community and to older people who may have developed a protective cross immunity against this virus due to past immunisations or previous natural influenza A H1N1 infections [8].

Half of the hospitalised patients presented classical predisposing chronic or immunosuppressive diseases, an observation that was also reported at the national level and which is consistent with previous studies [4–7]. The most common underlying conditions in our study were the presence of a pulmonary obstructive disorder and haematologic disorders.

A total of 85% of patients were treated by neuraminidase inhibitors. Nearly all adult patients received treatment, while not even 2/3 of the paediatric patients were treated. As the decision to introduce neuraminidase inhibitors was left to the discretion of the physician, it is difficult to preclude any conclusion from this different treatment's rate between adults and children. We can however hypothesise that less children received neuraminidase inhibitors because of a smaller proportion of risk factors for complications, milder symptoms and a spontaneously good evolution, especially if the diagnosis was made more than 48 hours after onset of symptoms.

A total of 16% of admitted patients had unfavourable outcomes requiring ICU admission for respiratory failure. These patients all had underlying conditions promoting influenza complications. We did not find significant predisposing risk factors associated with ICU admission, albeit presence of dyspnoea at diagnosis and haematological dis-

Table 1: Medical characteristics and underlying conditions of A H1N1 hospitalised patients.

	All patients (n = 85)	**Non-ICU patients (n = 71)**	**ICU patients (n = 14)**
Characteristics			
Median age – yr	39	34	56
Male sex – no (%)	45 (53)	38 (54)	7 (50)
Children <16 years – no (%)	29 (34)	26 (37)	3 (21)
Adults – no (%)	56 (66)	45 (63)	11 (79)
Underlying conditions – no (%)			
Chronic lung diseases	28 (32)	22 (31)	6 (43)
• Asthma	16 (19)	15 (21)	1 (7)
• COPD	13 (15)	9 (13)	4 (29)
• Lung fibrosis	2 (2)	1 (1)	1 (7)
• Kystic fibrosis	1 (1)	0 (0)	1 (7)
Immuno-suppression	19 (22)	13 (18)	6 (43)
• Haematologic disorder	9 (11)	5 (7)	4 (29)
• Active cancer	5 (6)	5 (7)	0 (0)
• Transplantation	2 (2)	1 (1)	1 (7)
• Immuno-suppressive therapy	11 (13)	7 (10)	4 (29)
• Auto-immune disease	4 (5)	4 (6)	0 (0)
Diabetes	9 (11)	9 (13)	0 (0)
Obesity (BMI >30)	12 (14)	12 (17)	0 (0)
Pregnancy	0 (0)	0 (0)	0 (0)
Previous or current smoker	42 (49)	37 (52)	5 (36)
Symptoms – no (%)			
• Cough	77 (91)	64 (91)	14 (100)
• Fever	72 (85)	62 (87)	10 (71)
• Rhinopharyngitis	40 (47)	35 (49)	5 (36)
• Dyspnoea	56 (66)	43 (61)	13 (93)
Mean length of stay – days (± SD)	12 (± 15.2)	7 (± 6.4)	11.3 (± 6.4)
Treatment – no (%)			
Anti-viral therapy	72 (85)	58 (82)	14 (100)
• Oseltamivir	72 (85)	58 (82)	14 (100)
• Zanamivir	6 (7)	1 (1)	5 (36)
Antibiotic treatment	37 (44)	23 (34)	13 (93)

order. These findings must be taken with caution considering the small sample of our study. Our rate of unfavourable outcomes including mortality was slightly inferior to the rates reported among hospitalised patients in North America [4, 6]. The relatively small size of our series limits further conclusions but we can highlight the high rate of anti-viral (85% overall but 100% in the ICU) and antibiotic treatment (44% of patients) as possible contributing factors.

Conclusion

The first weeks of Geneva's experience of the 2009 influenza A H1N1 pandemic showed a relatively moderate impact considering the number of affected cases, severe complications and deaths compared to initial influenza A H1N1 reports [1, 2, 4] and to seasonal influenza in Switzerland [9]. In comparison to seasonal influenza, the large majority of hospitalised patients were younger adults and children. Still for the first time, we systematically monitored the presence of influenza admission and could thus assess the real impact of influenza and subsequent complication like viral pneumonia in a Swiss University Hospital. This could be the basis to establish a systematic surveillance of influenza related hospitalisations during community outbreaks.

Study funding / potential competing interests

No financial support and no other potential conflict of interest relevant to this article was reported.

References

1 Echevarría-Zuno S, Mejía-Aranguré JM, Mar-Obeso AJ, Grajales-Muñiz C, Robles-Pérez E, González-León M, et al. Infection and death from influenza A H1N1 virus in Mexico: a retrospective analysis. Lancet. 2009;374(9707):2072–9.

2 WHO [homepage on the Internet]: Pandemic (H1N1) 2009 – update 78. [updated 2009 Dec 11]. Avalaible from: www.who.int/csr/disease/swineflu/fr/index.html

3 Swiss Federal Office for Public Health [homepage on the Internet]: Grippe pandémique (H1N1) 2009 en Suisse, semaines 17 (2009) à 8 (2010). [updated 2010 May 17]. Available from: http://www.bag.admin.ch/influenza/01120/01134/index.html?lang=fr

4 Jain S, Kamimoto L, Bramley AM, Schmitz AM, Benoit SR, Louie J, et al. Hospitalized Patients with 2009 H1N1 Influenza in the United States, April-June 2009. N Engl J Med. 2009;361(20):1935–44.

5 ANZIC Influenza Investigators, Webb SA, Pettilä V, Seppelt I, Bellomo R, Bailey M, Cooper DJ et al. Critical Care Services and 2009 H1N1 Influenza in Australia and New Zealand. N Engl J Med. 2009;361(20):1925–34.

6 Louie JK, Acosta M, Winter K, Jean C, Gavali S, Schechter R, et al. Factors associated with death or hospitalization due to pandemic 2009 Influenza A (H1N1) infection in California. JAMA. 2009;302(17):1896–902.

7 Kumar A, Zarychanski R, Pinto R, Cook DJ, Marshall J, Lacroix J, et al. Critically Ill Patients With 2009 Influenza A (H1N1) Infection in Canada, JAMA. 2009;302(17):1872–9.

8 Chowell G, Bertozzi SM, Colchero MA, Lopez-Gatell H, Alpuche-Aranda C, Hernandez M, et al. Severe respiratory disease concurrent with the circulation of H1N1 influenza, N Engl J Med. 2009;361(7):674–9.

9 Swiss Federal Office for Public Health [homepage on the Internet]: Grippe saisonnière 2008-2009: Epidémiologie, virologie, approvisionnement et composition du vaccin. [updated 2009 Jul 13]. Available from: http://www.bag.admin.ch/influenza/01118/01123/index.html?lang=fr