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Concurrent comparison of epidemiology, clinical presentation and outcome between adult patients suffering from the pandemic influenza A (H1N1) 2009 virus and the seasonal influenza A virus infection

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ABSTRACT

Purpose of study The demographics, clinical features and outcome of patients with pandemic influenza A (H1N1) 2009 infection were compared with a concurrent cohort of patients with seasonal influenza A infection.

Study design The clinical and microbiological data of hospitalised adult patients admitted between 29 June and 28 October 2009, with pandemic A (H1N1) 2009 or seasonal influenza A infection, were analysed.

Results A total of 186 patients including 69 pandemic A (H1N1) and 117 seasonal influenza were analysed. The majority (75%) under 50 years of age had pandemic A (H1N1). Compared with seasonal influenza, pandemic A (H1N1) patients were younger (median age 47 years vs 76 years, $p<0.001$), less likely to have lower respiratory tract symptoms (46.4% vs 66.7%, $p=0.007$), but more likely to be obese (5.8% vs 0%, $p=0.018$), pregnant (7.2% vs 0.9%, $p=0.027$) or have no underlying predisposing factors (24.6% vs 5.1%, $p<0.001$). Patients with pandemic A (H1N1) were more likely to receive oseltamivir (91.3% vs 40.2%, $p<0.001$), but less likely to receive antibiotics (75.4% vs 90.6%, $p=0.005$).

Respiratory failure was the reason for intensive care unit admission for all four patients with pandemic A (H1N1), but only for one of three patients with seasonal influenza. There were no statistical significant differences in the rate of intensive care unit admission or death.

Conclusions In addition to age, several clinical parameters were different between pandemic A (H1N1) and seasonal influenza. However, since both seasonal and pandemic influenza can lead to significant morbidity and mortality, the impact of pre-existing seasonal influenza should not be underestimated during the pandemic period.

INTRODUCTION

Pandemic influenza has been considered to cause greater morbidity and mortality than seasonal influenza, particularly among young adults.¹ In Mexico, the rate of severe pneumonia during the initial period of pandemic A (H1N1) 2009 was found to be much higher than in preceding years, with deaths predominantly occurring in the younger age group.² Another alarming feature of the current pandemic influenza is that >30% of patients with critical illness had no known predisposing conditions.³ A few studies involving paediatric patients have undertaken a more detailed comparison between the pandemic A (H1N1) 2009

and seasonal influenza. These studies have identified older children and those with underlying diseases to be found more frequently among hospitalised patients with pandemic A (H1N1) than those with seasonal influenza.^{4 5} The death rate of pandemic A (H1N1) among children and pregnant women is also higher than that of seasonal influenza from previous years.^{6 7} The major limitation of these studies is that historical data were used for comparison. Potential biases may arise when historical controls were used.⁸ For example, the threshold for hospital admission may vary during the pandemic and inter-pandemic period. There have been two studies in the southern hemisphere which concurrently compared pandemic A (H1N1) and seasonal influenza. The first study, conducted in Sydney, Australia, found that patients with pandemic A (H1N1) were younger and less likely to be immunocompromised than those with seasonal influenza.⁹ In that study, there were no statistically significant differences in the clinical features and outcome between pandemic A (H1N1) and seasonal influenza. In contrast, a study involving eight intensive care units (ICUs) in New South Wales, Australia, showed that the relative risk of admission to ICU of patients with pandemic A (H1N1) was 4.9 times higher than for those with seasonal influenza A infection.¹⁰

Pandemic A (H1N1) was first introduced into Hong Kong on 30 April 2009.¹¹ In this study, we sought to compare concurrently the epidemiology, clinical features, and outcome of hospitalised patients with pandemic and seasonal influenza. We chose to investigate patients hospitalised during the mitigation phase (started from 29 June 2009) to avoid including hospital admissions for isolation purpose only during the preceding containment phase of the pandemic.

METHODS

Patients

This retrospective study was approved by the institutional review board of the Hospital Authority of Hong Kong. Patients with laboratory confirmed influenza A virus infection were identified by the laboratory information system. Inclusion criteria were age 18 years or above; admission to our hospital during the 4 month period between 29 June to 28 October 2009; and positive reverse transcriptase-polymerase chain reaction (RT-PCR)

Original article

for influenza A virus *M* gene. We excluded patients electively admitted for other medical reasons.

Clinical data collection

Clinical information was obtained from the clinical management information system. Influenza-like illness was defined as the presence of fever and one of cough, sputum, sore throat or rhinorrhoea. Lower respiratory tract involvement was defined as subjective shortness of breath and physical findings of wheezing or crepitation. Cardiovascular complications were defined as acute coronary syndrome, congestive heart failure or arrhythmia. Acute respiratory distress syndrome (ARDS) and multiorgan failure were defined using standard criteria.^{12 13} Myositis is defined as elevation of creatine kinase >500 U/l without elevation of the MB isoenzyme or troponin.

Laboratory investigations

The diagnosis and subtyping of influenza A virus was performed by RT-PCR targeting the *M* gene, seasonal influenza A virus H1 and H3 gene, as previously described.^{11 14} Real-time one-step RT-PCR assays were used for the detection of pandemic A (H1N1) virus using Invitrogen SuperScript III Platinum One-Step Quantitative Kit in a 7500 Sequence Detection System (Applied Biosystem, Foster City, CA, USA). Briefly, 5 µl purified RNA was amplified in a 25 µl reaction containing 0.5 µl SuperScript III Reverse Transcriptase/Platinum Taq DNA polymerase (Invitrogen), 0.05 µl ROX reference dye (25 µM), 12.5 µl of 2X reaction buffer, 800 nmol/l forward primer (5'-CCAAAGCT-CAGCAAATCCTACAT-3'), corresponding to nucleotides 526 to 548, 800 nmol/l reverse primer (5'-GATGGTGAATGCCCCA-TAGC-3'), corresponding to nucleotides 576 to 595), and probe 200 nmol/l (Fam-TGATAAAGGGAAAGAAGTCCT-MGB), corresponding to nucleotides 552 to 572, designed by multiple alignment of the HA gene sequences of swine H1 virus and the pandemic influenza A/California/04/2009 (available in GenBank). Positive control experiments with a pandemic A (H1N1) virus (A/California/04/2009) and negative control experiments with seasonal A (H1N1) and A (H3N2) viruses were performed. Reactions were first incubated at 50°C for 30 min, followed by 95°C for 2 min, and were then thermal cycled for 50 cycles (95°C for 15 s, 55°C for 30 s).

Viral load was determined by quantitative RT-PCR of the influenza A virus *M* gene.¹⁵ Direct antigen detection by immunofluorescence using IMAGEN respiratory screen and typing reagents (Oxoid Ely Ltd, Ely, Cambridgeshire, UK) and viral culture using Madin–Darby canine kidney cell monolayer in culture tubes was performed as described elsewhere.^{16 17}

Data analysis

For comparison of pandemic and seasonal influenza, χ^2 or Fisher's exact test were used for categorical variables, whereas Mann–Whitney U test or independent sample t test were used for continuous variables where appropriate. Multivariate logistic regression was performed to identify factors independently associated with the type of influenza. SPSS 17.0 for Windows (SPSS Inc, Chicago, Illinois, USA) was used for statistical computation. A value of $p < 0.05$ was considered to represent significant difference.

RESULTS

Patient profile

A total of 186 adult patients were included in this study, with 69 patients infected with the pandemic A (H1N1) 2009 virus, 20 patients with seasonal A (H1) virus, and 97 patients with

seasonal A (H3) virus. By comparison, data from the Centre for Health Protection in Hong Kong showed that seasonal influenza virus was isolated from 7366 specimens (6280 H3N2 and 1086 seasonal H1N1 virus), and pandemic A (H1N1) virus was isolated from 22974 specimens, between July and October 2009.¹⁸ In September 2009, there was a sharp increase in the incidence of influenza A in Hong Kong, mainly related to an increase in pandemic A (H1N1) virus and to a lesser extent the seasonal influenza virus H3N2.¹⁹

The majority (39/52, 75%) of patients below the age of 50 years were infected with pandemic A (H1N1), but admissions for seasonal influenza predominated in the age group above 50 (figure 1). The median age of patients with pandemic A (H1N1) was significantly younger than those with seasonal influenza ($p < 0.001$) (table 1). In general, patients with pandemic A (H1N1) were less likely to have underlying predisposing factors than those with seasonal influenza ($p < 0.001$). Specifically, hypertension ($p < 0.001$) or chronic neurological impairment ($p = 0.003$) were less common. However, obese ($p = 0.018$) or pregnant patients ($p = 0.027$) were more common in the pandemic A (H1N1) cohort. There was no statistical difference between reasons for hospital admission (table 2). Among pregnant women with pandemic A (H1N1), one had a spontaneous miscarriage and another had a threatened miscarriage. One pregnant woman with seasonal influenza was hospitalised for decreased fetal movement. Younger age, obesity, and absence of chronic neurological impairment were shown to be independent underlying factors associated with pandemic A (H1N1) by multivariate logistic regression.

Clinical features

Symptoms of influenza-like illness were more frequent in patients with pandemic A (H1N1), although this did not reach statistical significance ($p = 0.156$) (table 2). Gastrointestinal symptoms (vomiting or diarrhoea) were also more frequent in patients with pandemic A (H1N1), almost reaching statistical significance ($p = 0.050$). Clinical features of lower respiratory tract involvement were less common among patients with pandemic A (H1N1) ($p = 0.007$), but there was no significant difference in the frequency of pulmonary infiltrate on chest radiograph. There was a wide spectrum of chest radiographic findings in both groups of patients, which can present as lobar consolidation, diffuse alveolar opacities or acute pulmonary oedema (figures 2–4).

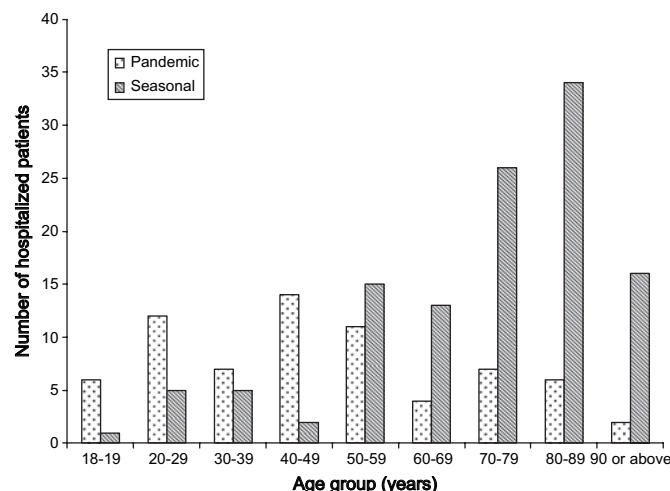


Figure 1 Age distribution of hospitalised patients infected with pandemic influenza A (H1N1) virus and seasonal influenza virus.

Table 1 Comparison of demographics and underlying predisposing factors between patients with pandemic A (H1N1) and seasonal influenza

	Pandemic A (H1N1) (n=69)	Seasonal influenza (n=117)	p Value*
Demographics			
Male sex	29 (42.0)	61 (52.1)	0.183
Age	47 (29–63)	76 (60–86)	<0.001
Underlying predisposing factors			
Hypertension	16 (23.2)	61 (52.1)	<0.001
Chronic heart disease	10 (14.5)	31 (26.5)	0.056
Chronic lung disease	18 (26.1)	34 (29.1)	0.663
Chronic liver disease	4 (5.8)	6 (5.1)	1.000†
Chronic renal disease	6 (8.7)	9 (7.7)	0.808
Connective tissue disease	2 (2.9)	2 (1.7)	0.628†
Chronic neurologic impairment	4 (5.8)	26 (22.2)	0.003
Diabetes mellitus	12 (17.4)	27 (23.1)	0.357
Malignancy	11 (15.9)	19 (16.2)	0.958
HIV infection	0 (0)	1 (0.9)	1.000†
Transplant	4 (5.8)	3 (2.6)	0.427†
Use of immunosuppressive drugs	6 (8.7)	6 (5.1)	0.366†
Smoker	9 (13.0)	26 (22.2)	0.122
Obesity	4 (5.8)	0 (0)	0.018†
Pregnancy	5 (7.2)	1 (0.9)	0.027†
No known predisposing factors	17 (24.6)	6 (5.1)	<0.001

Data are presented as median (interquartile range) for continuous variable, and no. (%) for categorical variables.

* χ^2 test was used for categorical variable and Mann–Whitney U test was used for continuous variables unless otherwise stated.

†By Fisher's exact test.

Oseltamivir was prescribed more frequently to patients with pandemic A (H1N1), but antibiotics were prescribed more frequently to those with seasonal influenza.

Laboratory investigations

Elevated alanine transaminase ($p=0.020$) and creatinine ($p=0.004$) concentrations were more common in patients with pandemic A (H1N1) (table 3). Viral culture was performed for all seasonal A (H1) cases and 95 (97.9%) cases of seasonal A (H3), with all positive viral cultures being A (H1N1) and A (H3N2), respectively. Positive viral culture was more frequent in the patients with pandemic A (H1N1) than seasonal influenza ($p=0.025$) (table 4), and the difference was mainly related to a lower rate of positive viral culture for seasonal A (H3N2). There was no significant difference in the positive rate of direct immunofluorescence or viral load. Two patients with pandemic A (H1N1) (*Bacillus* species, coagulase negative *Staphylococcus*) and one patient with seasonal influenza (*Micrococcus* species) had positive blood culture, but all isolates were considered to be contamination. There was no statistically significant difference in the total number of positive sputum culture and bacterial isolates between the two groups.

Intensive care admissions

Four patients with pandemic A (H1N1) infection were admitted to the ICU. Three of them were admitted due to respiratory failure from viral pneumonitis, two of whom developed ARDS. The fourth patient, with end stage renal failure, was admitted to the ICU due to acute pulmonary oedema. Of the patients with seasonal influenza, one patient with a history of asthma was admitted to the ICU due to severe infective exacerbation. Another patient, a 26-year-old man with good past health, was

Table 2 Comparison of reason of admission, clinical features, treatment and outcome between patients with pandemic A (H1N1) and seasonal influenza

	Pandemic A (H1N1) (n=69)	Seasonal influenza (n=117)	p Value*
Days of symptoms before admission	2 (1–3)	1 (1–3)	0.059
Duration of hospitalisation	4 (2–7)	3 (2–6)	0.224
Reason for admission			
Pulmonary symptoms	47 (68.1)	85 (72.6)	0.511
Neurological symptoms	5 (7.2)	13 (11.1)	0.389
Other symptoms	17 (24.6)	19 (16.2)	0.161
Exacerbation of underlying disease			
Pulmonary disease	10 (14.5)	24 (20.5)	0.305
Other diseases	5 (7.2)	12 (10.3)	0.491
Vital signs at admission and emergency department			
Hypotension‡	16 (23.2)	19 (16.2)	0.241
Pulse >100/min	32 (46.4)	48 (41.0)	0.476
Respiratory rate >20/min	14 (20.3)	28 (23.9)	0.566
Temperature $\geq 38^\circ\text{C}$	34 (49.3)	62 (53.0)	0.624
Oxygen saturation <90% while breathing ambient air	12 (17.4)	34 (29.1)	0.075
Clinical features			
Influenza-like illness	58 (84.1)	88 (75.2)	0.156
Subjective fever	62 (89.9)	96 (82.1)	0.151
Sore throat or rhinorrhoea	47 (68.1)	63 (53.8)	0.056
Cough or sputum	59 (85.5)	103 (88.0)	0.619
Lower respiratory tract symptoms	32 (46.4)	78 (66.7)	0.007
Dyspnoea	27 (39.1)	55 (47.0)	0.296
Wheezing	11 (15.9)	29 (24.8)	0.156
Crepitation	25 (36.2)	49 (41.9)	0.447
Pulmonary infiltrate on chest radiograph	25 (36.2)	52 (44.4)	0.272
Vomiting or diarrhoea	15 (21.7)	13 (11.1)	0.050
Treatment			
Oseltamivir	63 (91.3)	47 (40.2)	<0.001
Days of symptoms before oseltamivir	3 (2–5)	3 (1–4)	0.252
Zanamivir	4 (5.8)	1 (0.9)	0.064†
Antibiotics	52 (75.4)	106 (90.6)	0.005
Complications			
Cardiovascular	6 (8.7)	10 (8.5)	0.972
Acute respiratory distress syndrome	2 (2.9)	0 (0)	0.136†
Multiorgan failure	1 (1.4)	2 (1.7)	1.000†
Myositis	0 (0)	2 (1.7)	0.531†
ICU admission	4 (5.8)	3 (2.6)	0.427†
Duration of ICU stay (days)	2.12 (0.84–11.87)	0.96 (0.59–2.81)	0.289
Positive pressure ventilation§	4 (5.8)	4 (3.4)	0.472†
Death	2 (2.9)	7 (6.0)	0.488†
Days of symptoms before death	21 (11–31)	11 (6–21)	0.372

Data are presented as median (interquartile range) for continuous variable, and no. (%) for categorical variables.

* χ^2 test was used for categorical variable and Mann–Whitney U test was used for continuous variables unless otherwise stated.

†By Fisher's exact test.

‡Systolic blood pressure <90 mm Hg or diastolic blood pressure <60 mm Hg.

§Include mechanical ventilation, bilevel positive airway pressure support, and continuous positive airway pressure support.

ICU, intensive care unit.

admitted to the ICU for close monitoring due to generalised weakness and oxygen desaturation, but spontaneously recovered and stayed in the ICU for only 14 h. The third patient was

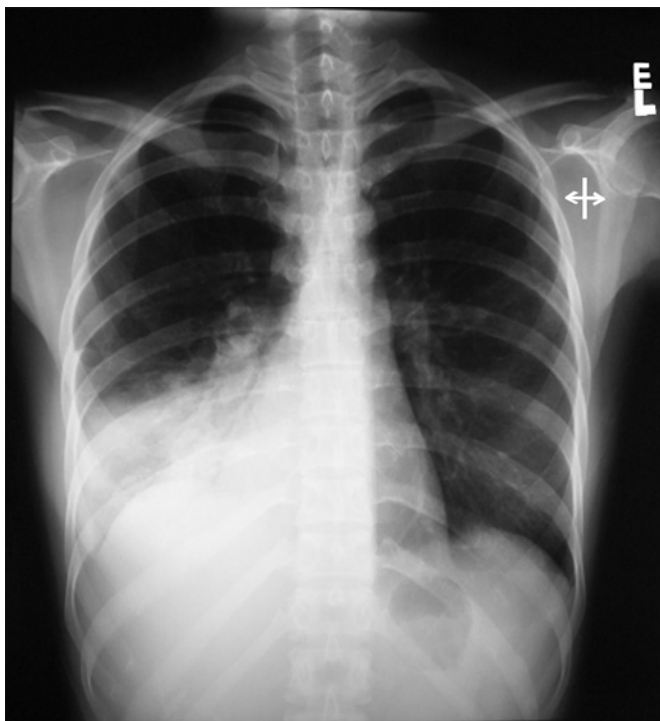


Figure 2 Chest radiograph of a patient with good past health, showing right lower zone consolidation.

admitted with acute perforated duodenal ulcer, and was transferred to the ICU for postoperative care. There was no significant difference in mortality rate between patients with pandemic A (H1N1) and those with seasonal influenza.

DISCUSSION

This study concurrently compared pandemic A (H1N1) with seasonal influenza for hospitalised adult patients. In contrast to seasonal influenza, those patients with pandemic A (H1N1) were significantly younger and less likely to have underlying predisposing factors, but were more likely to be obese or pregnant. Gastrointestinal symptoms were more frequent in patients with pandemic A (H1N1), but lower respiratory tract symptoms were less common. Patients with seasonal influenza were less likely to receive antiviral treatment.

As predicted from previous studies using seasonal influenza historical controls² and those of previous pandemics,¹ our study

has confirmed that patients with pandemic A (H1N1) are indeed younger than those with seasonal influenza. The age difference may be explained by the lack of cross-reactive antibody in the younger population.²⁰ On the other hand, the absolute number of admissions was higher for patients with seasonal influenza, especially those age 50 years or above. As a comparison, the total number of pandemic A (H1N1) isolated by the Public Health Laboratory Centre of Hong Kong, which receive clinical specimens from both community and hospitalised patients in the entire Hong Kong Special Administrative Region, exceed that of seasonal influenza by more than threefold.¹⁸ The large number of hospital admissions due to seasonal influenza is related to seasonal A (H3), and may be due to the emergence of A/Perth/16/2009, which is antigenically distinct from the current vaccine strain A/Brisbane/10/2007 and A/Uruguay/716/2007.²¹ Therefore, the burden on hospitals due to seasonal influenza during the pandemic period should not be underestimated.

Our results have shown that underlying diseases were more frequent in patients with seasonal influenza, especially hypertension and chronic neurological impairment. Since these factors may be associated with older age, we performed multivariate logistic regression analysis, and found that only chronic neurological impairment remained significantly associated with seasonal influenza. As bidirectional neural-immune communication is an important aspect of the innate immune system, damage to the brain can affect the immune response to infections, as has been demonstrated in patients with stroke.²²

A case-control study has found obesity to be a risk factor for severe presentations of pandemic A (H1N1), which has not been described for seasonal influenza.²³ In our study, obese patients were over-represented in hospitalised patients with pandemic A (H1N1) when compared with seasonal influenza, although the absolute number was small. In Hong Kong, the obese population is relatively small, and may explain the lower rate of obesity in our cohort when compared to those in western countries.²⁴ In addition to obesity, we have also identified pregnancy as being more common among patients with pandemic A (H1N1) than seasonal influenza, although multivariate logistic regression analysis suggests that this may be related to age. Pregnancy is a widely accepted risk factor for complications in both pandemic and seasonal influenza,²⁵ and studies have found that the maternal death rate of pandemic A (H1N1) exceeds that of seasonal influenza in preceding years.⁷ Documented fetal complications of influenza include spontaneous abortion, preterm premature rupture of membrane, and preterm labour.²⁵

Figure 3 Chest radiographs of a patient admitted for diabetic ketoacidosis.

(A) Chest radiograph was taken on admission, showing early left lower zone infiltration. (B) Rapid progression to bilateral diffuse panlobar involvement (chest radiograph taken 20 h after the radiograph shown in panel A).

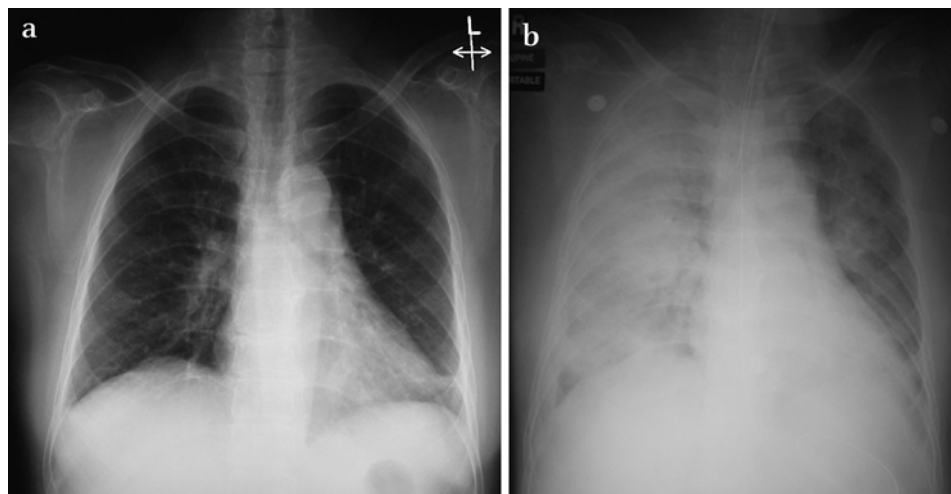
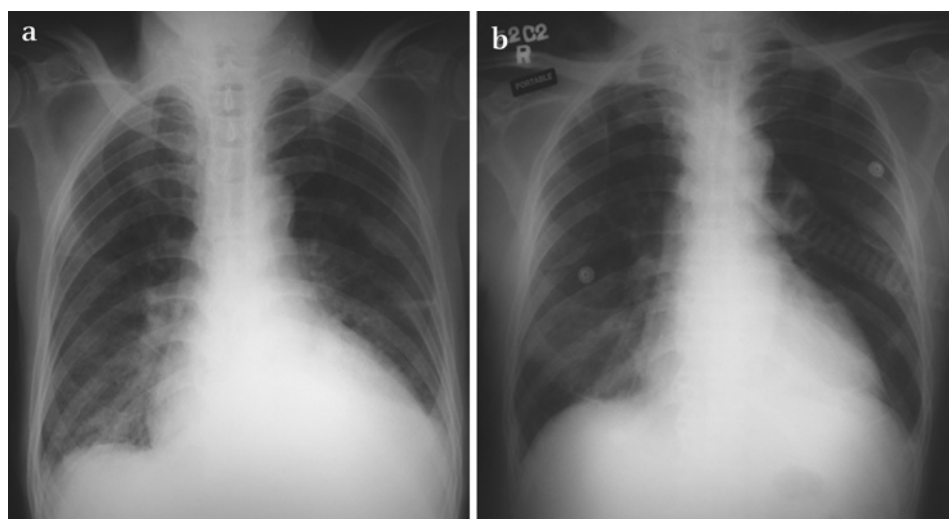


Figure 4 Chest radiographs of a patient with congestive heart failure and end stage renal failure due to diabetic nephropathy. (A) Chest radiograph taken on admission, showing acute pulmonary oedema. (B) Persistent right lower zone infiltrates after diuresis.



It has been shown that influenza virus can infect the placenta,²⁶ and in a recent study influenza virus was shown to replicate in first trimester trophoblast cell lines.²⁷

In contrast to the study conducted by Chang *et al*,⁹ which is also a concurrent analysis of hospitalised patients with pandemic A (H1N1) and seasonal influenza, our study found several differences in the clinical features of patients with pandemic A (H1N1) and seasonal influenza. This may be because our study included more patients, allowing detection of smaller differences. Another factor is that there may be differences in the criteria for hospital admissions. In our cohort, patients with seasonal influenza were more likely to have lower respiratory tract symptoms, but there was no statistical

difference in the frequency of pulmonary infiltrates on chest radiograph. One possibility is that older patients are more susceptible to acute bronchitis after viral infection. On the other hand, diarrhoea or vomiting were also more common among patients with pandemic A (H1N1), almost reaching statistical significance. Although the exact pathogenic mechanism of gastrointestinal symptoms remains uncertain, this is consistent with the results of an *in vitro* study which demonstrated that more severe cytopathic effect, immunostaining and greater viral replication occurred in intestinal cell lines for pandemic A (H1N1) virus than seasonal influenza A virus.²⁸ Despite comparable rates of chronic liver and renal disease, elevated values of both alanine transaminase and creatinine were found more frequently in patients with pandemic A (H1N1), which may represent a predilection for the systemic involvement of pandemic A (H1N1) virus.

In another study using concurrent analysis of pandemic and seasonal influenza, it has been shown that there is a higher risk of ICU admission from pandemic A (H1N1) than seasonal influenza.¹⁰ However, this has not been observed in our study, and is likely related to major differences in methodology. In their study, the denominator for the rate of ICU admission was the total number of specimens tested positive for influenza A. However, they did not specify whether these specimens were collected from hospitalised patients or outpatients. In our study, on the other hand, the denominator for the rate of ICU admission was the number of hospitalised patients only. Furthermore, we have also analysed the differences in the reasons for admission to ICU. All four patients with pandemic A (H1N1), but only one patient with seasonal influenza, were admitted to the ICU due to severe respiratory distress. Among those infected with pandemic A (H1N1), two had ARDS. This finding is compatible with animal models suggesting more severe involvement of the lower respiratory tract in pandemic A (H1N1) than seasonal influenza virus infection.²⁰

Oseltamivir were more frequently prescribed in patients with pandemic A (H1N1), probably due to the perceived higher risk of complications in this group of patients. However, most studies of oseltamivir were performed in patients with seasonal influenza, and it was shown that treatment with an antiviral reduced the mortality rate in hospitalised patients with seasonal influenza.²⁹ On the other hand, antibiotics were more frequently given to patients with seasonal influenza, although the rate of laboratory confirmed bacterial pneumonia was not statistically different. This could be due to the higher frequency of lower

Table 3 Comparison of selected laboratory tests between patients with pandemic A (H1N1) and seasonal influenza

	Pandemic A (H1N1) no./total no. (%)	Seasonal influenza no./total no. (%)	p Value*
Blood tests			
Leucocytosis ($>10.1 \times 10^9/l$)	16/67 (23.9)	33/116 (28.4)	0.501
Neutrophilia ($>6.7 \times 10^9/l$)	26/67 (38.8)	45/116 (38.8)	0.999
Lymphopenia ($<1.2 \times 10^9/l$)	52/67 (77.6)	94/116 (81.0)	0.579
Thrombocytopenia ($<170 \times 10^9/l$)	26/67 (38.8)	51/116 (44.0)	0.496
Elevated alanine transaminase (>36 IU/l)	17/66 (25.8)	14/115 (12.2)	0.020
Elevated creatinine (>82 μ mol/l)	25/66 (37.9)	69/115 (60.0)	0.004
Elevated creatine kinase (>161 IU/l)	9/37 (24.3)	18/54 (33.3)	0.355
Positive sputum culture			
<i>Streptococcus pneumoniae</i>	8/37 (21.6)	14/60 (23.3)	0.845
<i>Staphylococcus aureus</i>	1	2	1.000†
<i>Haemophilus influenzae</i>	1	0	0.371†
<i>Moraxella catarrhalis</i>	1	2	1.000†
<i>Klebsiella</i> species	1	0	0.371†
<i>Pseudomonas aeruginosa</i>	2	1	0.556†
Others	2	4	1.000†
Others	0	5‡	0.159†

Data are presented as median (interquartile range) for continuous variable, and no. (%) for categorical variables.

* χ^2 test was used for categorical variable and Mann–Whitney U test was used for continuous variables unless otherwise stated.

†By Fisher's exact test.

‡*Flavobacterium* species (1), *Escherichia coli* (1), *Candida* species (2), β -haemolytic *Streptococcus* and *Candida* species (1).

Table 4 Comparison of the virology profile of pandemic A (H1N1) and seasonal influenza virus infection

	Pandemic A (H1N1)	Seasonal influenza	p Value*
Mean viral load \pm 1 SD [¶] (log ₁₀ M gene copies/ml)	5.97 \pm 1.62	6.11 \pm 1.32	0.553
		Seasonal A (H1N1): 6.53 \pm 1.33	0.189†
		Seasonal A (H3N2): 6.02 \pm 1.31	0.810‡
Positive direct antigen detection by immunofluorescence, no./total no. (%)	43/65 (66.2)	86 /115 (74.8)	0.217
		Seasonal A (H1): 16/19 (84.2)	0.130†
		Seasonal A (H3): 70/96 (72.9)	0.357‡
Positive viral culture, no./total no. (%)	55/65 (84.6)	80/115 (69.6)	0.025
		Seasonal A (H1N1): 16/20 (80)	0.731† §
		Seasonal A (H3N2): 64/95 (67.3)	0.014‡

* χ^2 test was used for categorical variable and independent sample t test was used for continuous variables unless otherwise stated.

†Comparison between pandemic A (H1N1) and seasonal A (H1N1).

‡Comparison between pandemic A (H1N1) and seasonal A (H3N2).

§By Fisher's exact test.

¶Viral load was available for 55 patients with pandemic A (H1N1), 111 patients with seasonal influenza (18 patients with seasonal A (H1N1) and 93 patients with seasonal A (H3N2)).

respiratory tract symptoms in patients with seasonal influenza. Previous studies showed that patients with acute bronchitis were more likely to be treated with antibiotics than patients with upper respiratory tract infections.³⁰

Limitations

There are several limitations in our study. First, we have only included adult patients, and therefore our findings cannot be generalised to the whole population. If we included children, the difference in age may even be greater because previous studies have shown that children hospitalised for pandemic A (H1N1) are older than those for seasonal influenza.⁴ Secondly, only hospitalised patients were analysed in this study. The threshold for admission may be influenced by age or underlying diseases. Thirdly, as in all retrospective studies, all clinical information was based on reviewing of clinical records. Some symptoms may be missed because the attending physician did not elicit such a history. However, because the diagnosis was not known at admission for most patients, these problems affected all patients

with pandemic and seasonal influenza. Another potential limitation in our study is that body height and body weight were not recorded for most patients, and therefore some patients with obesity may have been missed. Because antiviral treatment was more frequently given to patients with pandemic H1N1, this should theoretically improve the outcome of such patients, and may affect the interpretation on the differences in outcome between pandemic and seasonal influenza. Finally, the relatively small sample size prohibited the detection of small differences between the two groups.

Conclusion

By evaluating patients with pandemic and seasonal influenza hospitalised during the same period, this study allowed us to provide an unbiased view on the differences between infections caused by these two types of influenza virus subtypes. Though pandemic influenza causes great concern, especially among healthy young adults, the impact of seasonal influenza should not be overlooked.

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Main messages

- ▶ Patients with pandemic A (H1N1) virus infection are younger, more likely to be obese, or pregnant, and less likely to have underlying predisposing factors than those with seasonal influenza.
- ▶ Seasonal influenza can lead to significant morbidity and mortality during the pandemic period, and the impact should not be underestimated.

Current research questions

- ▶ What is the difference in demographics, clinical features and outcomes between pandemic A (H1N1) and seasonal influenza in the community setting?
- ▶ Why are obese patients more likely to develop complications due to influenza?

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