

1-1-2011

Analysis of 113 hospitalized patients with confirmed 2009 influenza A (H1N1) virus infection

ESRAGÜL AKINCI

BİRCAN KAYAASLAN

MELTEM ARZU YETKİN

SEVİM YILMAZ

İŞİL DENİZ ALIRAVCI

See next page for additional authors

Follow this and additional works at: <https://journals.tubitak.gov.tr/medical>

 Part of the [Medical Sciences Commons](#)

Recommended Citation

AKINCI, ESRAGÜL; KAYAASLAN, BİRCAN; YETKİN, MELTEM ARZU; YILMAZ, SEVİM; ALIRAVCI, İŞİL DENİZ; YILDIZ, SÜMEYYE; ÜLGEN, FATMANUR; EREN, SELİM SIRRI; BUT, AYŞE; YILMAZ, GÜLRUHSAR; KILCI, OYA; MUTLU, NEVZAT MEHMET; YAĞMURDUR, HATİCE; and BODUR, HURREM (2011) "Analysis of 113 hospitalized patients with confirmed 2009 influenza A (H1N1) virus infection," *Turkish Journal of Medical Sciences*: Vol. 41: No. 3, Article 19. <https://doi.org/10.3906/sag-1003-688>
Available at: <https://journals.tubitak.gov.tr/medical/vol41/iss3/19>

This Article is brought to you for free and open access by TÜBİTAK Academic Journals. It has been accepted for inclusion in Turkish Journal of Medical Sciences by an authorized editor of TÜBİTAK Academic Journals. For more information, please contact academic.publications@tubitak.gov.tr.

Analysis of 113 hospitalized patients with confirmed 2009 influenza A (H1N1) virus infection

Authors

ESRAGÜL AKINCI, BİRCAN KAYAASLAN, MELTEM ARZU YETKİN, SEVİM YILMAZ, İŞİL DENİZ ALIRAVCI, SÜMEYYE YILDIZ, FATMANUR ÜLGEN, SELİM SIRRI EREN, AYŞE BUT, GÜLRUHSAR YILMAZ, OYA KILCI, NEVZAT MEHMET MUTLU, HATİCE YAĞMURDUR, and HURREM BODUR

Analysis of 113 hospitalized patients with confirmed 2009 influenza A (H1N1) virus infection

Esragül AKINCI¹, Bircan KAYAASLAN¹, Meltem Arzu YETKİN¹, Sevim YILMAZ¹, Işıl Deniz ALIRAVCI¹, Sümeyye YILDIZ¹, Fatmanur ÜLGEN¹, Selim Sırrı EREN¹, Ayşe BUT¹, Gülruhsar YILMAZ¹, Oya KILCI², Nevzat Mehmet MUTLU², Hatice YAĞMURDUR², Hürrem BODUR¹

Aim: To evaluate the demographic characteristics, clinical and laboratory features, underlying medical conditions, treatment, and outcome of hospitalized patients with laboratory-confirmed infection due to the 2009 influenza A(H1N1) virus.

Materials and methods: This prospective study was performed between October and December 2009. The hospitalized patients with laboratory-confirmed diagnosis of 2009 influenza A(H1N1) virus infection were included in the study. The diagnosis was confirmed with detection of the virus in nasal and nasopharyngeal swabs by RT-PCR assay. Demographic and epidemiological characteristics, clinical features, treatment, and outcome of the patients were recorded on the individual forms. A comparison was made between patients with and without pneumonia.

Results: From October to December 2009, 113 confirmed patients with 2009 influenza A(H1N1) virus infection were hospitalized in our clinic. The ages of the patients were between 17 and 77 years (mean age 35.7 ± 15.8 years) and 73 (64.6%) were female. Cough (92.9%), fever (85.8%), malaise (85.8%), headache (80.5%), and muscle aches (85.0%) were the most common presenting symptoms. The time from symptom onset to hospital admission was 1-15 days (mean time 3.8 ± 3 days). On physical examination, fever (74.3%), pharyngeal hyperemia (66.4%), rales (43.4%), dyspnea (29.2%), and cyanosis (4.4%) were the presenting clinical findings. Of the patients, 64 (56.6%) had at least 1 underlying medical condition. The most common underlying disease was chronic pulmonary disease (14.5%). A total of 25 patients were pregnant. On admission to hospital, 25 patients (22.1%) had leukopenia, 12 patients (10.6%) had leukocytosis, and 29 patients (25.7%) had thrombocytopenia. Pulmonary infiltrates consistent with pneumonia were detected on chest radiography in 47 (41.6%) patients. Of these patients, 98 (86.7%) received oseltamivir treatment on admission. Six patients (5.3%) were admitted to the ICU because of acute respiratory failure and 4 of them (3.5%) required mechanical ventilation. Among these patients, 3 (2.7%) died. A comparison between the patients with and without pneumonia was performed statistically. Age older than 40 years old, time from onset of symptoms to admission longer than 3 days, leukocytosis, ALT/AST elevation, and hyperglycemia were significantly higher in patients with pneumonia.

Conclusion: Although the 2009 influenza A(H1N1) virus causes severe illness including pneumonia and death, the mortality rate is not very high. The characteristics of the disease are similar to those of seasonal influenza. Young adults were the most affected persons and most of the patients had underlying medical conditions.

Key words: Influenza, H1N1, flu

Received: 10.03.2010 – Accepted: 24.09.2010

¹ Department of Infectious Diseases and Clinical Microbiology, Ankara Numune Education and Research Hospital, Ankara - TURKEY

² Department of Anesthesiology and Reanimation, Ankara Numune Education and Research Hospital, Ankara - TURKEY

Correspondence: Esragül AKINCI, Department of Infectious Diseases and Clinical Microbiology, Ankara Numune Education and Research Hospital, 06100 Samanpazari, Ankara - TURKEY
E-mail: esragulakinci@yahoo.com

2009 influenza A (H1N1) enfeksiyonu tanısıyla yatırılan 113 hastanın analizi

Amaç: Bu çalışmanın amacı, 2009 influenza A(H1N1) kesin tanısı konulan ve yatırılarak takip edilen hastaların demografik özellikleri, klinik ve laboratuvar bulguları, altta yatan hastalıkları, tedavi ve prognozunu değerlendirmektir.

Yöntem ve gereç: Bu prospektif çalışma Ekim-Aralık 2009 tarihleri arasında yapıldı. 2009 influenza A(H1N1) tanısı kesinleşmiş yatan hastalar çalışmaya alındı. Tanı, nazal ve nazofaringeal sürüntü örneklerinde RT-PCR ile virüs tespit edilerek konuldu. Hastaların demografik ve epidemiyolojik özellikleri, klinik bulguları, tedavi ve prognozu hazırlanan hasta formlarına kaydedildi. Pnömonisi olan ve olmayan hastalar arasında karşılaştırma yapıldı.

Bulgular: Ekim-Aralık 2009 arasında, 2009 influenza A(H1N1) enfeksiyonu tanısıyla 113 hasta kliniğimizde yatırılarak takip edildi. Hastaların yaşları 17-77 (ortalama $35,7 \pm 15,8$) arasında değişmekte idi ve 73'ü (% 64,6) kadındı. En sık görülen semptomlar, öksürük (% 92,9), ateş (% 85,8), halsizlik (% 85,8), baş ağrısı (% 80,5) ve kas ağrısı (% 85) idi. Hastaneye yatışa kadar olan semptomların süresi 1-15 gün (ortalama $3,8 \pm 3$) arasında değişmekteydi. Fizik muayenede ateş (% 74,3), faringeal hiperemi (% 66,4), ral (% 43,4), dispne (% 29,2) ve siyanoz (% 4,4) tespit edildi. Hastaların 64'ünde (% 56,6) altta yatan en az bir hastalık vardı ve en sık tespit edilen kronik akciğer hastalığı (% 14,5) idi. Gebelik 25 hastada mevcuttu. Yatışta 25 hastada (% 22,1) lökopeni, 12 hastada (% 10,6) lökositoz ve 29 hastada (% 25,7) trombositopeni tespit edildi. Akciğer grafisinde pnömoni ile uyumlu infiltrasyonlar 47 (% 41,6) hastada saptandı. Oseltamivir 98 (% 86,7) hastaya verildi. Hastaların 6'sı (% 5,3) akut solunum yetmezliği nedeniyle yoğun bakım ünitesine kabul edildi ve 4'ü (% 3,5) mekanik ventilator bağlandı. Üç hasta (% 2,7) kaybedildi. Pnömonisi olan ve olmayan hastalar istatistiksel olarak karşılaştırıldı. Yaşın 40'in üzerinde olması, semptomların süresinin 3 günden fazla olması, lökositoz, ALT/AST yüksekliği ve hiperglisemi, pnömonisi olanlarda anlamlı oranda yüksek bulundu.

Sonuç: 2009 influenza A(H1N1) enfeksiyonu, pnömoni ve ölüm gibi ciddi tablolara yol açsa da mortalite oranı çok yüksek değildir. Hastalığın özellikleri mevsimsel influenza gibidir. Genç erişkinler en çok etkilenen kişilerdir ve çoğunda altta yatan hastalık vardır.

Anahtar sözcükler: Influenza, H1N1, grip

Introduction

Human infection with the novel influenza A(H1N1) virus was first reported in April 2009 in Mexico and then it spread to the United States and other countries in the world (1,2). On 11 June 2009 the World Health Organization (WHO) raised the pandemic alert to 'Phase 6', which is the highest alert level (3).

The 2009 influenza A(H1N1) virus represents a reassortment of human, avian, and swine influenza viruses (4). The infection with 2009 influenza A(H1N1) generally presents mild disease with symptoms similar to those of seasonal influenza A. Young adults are the most affected people. The hospitalization rate is up to 10% among confirmed cases. A significant proportion of hospitalized patients have pneumonia. The presence of underlying diseases poses a greater risk of death, and mortality is below 1%. The most common causes of death are pneumonia and acute respiratory distress syndrome (ARDS) (5-7).

In this report, we describe the demographic characteristics, clinical and laboratory features, underlying medical conditions, treatment, and outcome of hospitalized patients with laboratory-

confirmed infection due to the 2009 influenza A(H1N1) virus.

Materials and methods

This prospective study was performed between October and December 2009. The hospitalized patients with laboratory-confirmed diagnosis of 2009 influenza A(H1N1) virus infection were included in the study.

The patients admitted to our hospital with symptoms of influenza-like illness (fever, sore throat, or cough) were evaluated for hospitalization. On admission, blood analyses were performed in all patients and the non-pregnant ones underwent chest radiography. Patients with underlying medical conditions (pregnancy, obesity, chronic pulmonary disease, cardiovascular diseases, malignancy, diabetes mellitus etc.), pulmonary infiltrates on chest radiography, or severe clinical presentation were hospitalized. Severe cases were defined in patients admitted to an intensive care unit (ICU), requiring mechanical ventilation, presenting signs of respiratory failure (tachypnea, cyanosis or hypoxia

with oxygen saturation below 90%), or having severe vomiting or hypotension (systolic blood pressure below 90 mmHg). Nasal and nasopharyngeal swabs were performed from all of the hospitalized patients and only confirmed cases were included in the study.

The diagnosis was confirmed with detection of 2009 influenza A(H1N1) virus in nasal and nasopharyngeal swabs by real-time reverse-transcriptase-polymerase-chain reaction (RT-PCR) assay. All RT-PCR tests were performed at Refik Saydam National Public Health Agency, Virology Reference and Research Laboratory.

On admission, oseltamivir treatment was recommended to all of the patients, including pregnant women. Except for some pregnant women, all of the patients agreed to receive it. Oseltamivir was given for 5 days at a dose of 75 mg twice daily. The patients with pulmonary infiltrates on chest radiography, leukocytosis, or symptoms of acute sinusitis or exacerbation of chronic obstructive pulmonary disease (COPD) were given empirical antibiotic treatment. Before initiation of antibiotics, blood cultures were performed. Most of the patients could not expectorate. Thus, sputum cultures were done in very few patients. Oxygen saturations of the patients were measured by pulse oxymetry periodically from admission to discharge.

Demographic and epidemiological characteristics, clinical features, laboratory and radiographic findings, underlying medical conditions, treatment, and outcome of the patients were recorded on the individual forms. A comparison was made between patients with and without pneumonia. Statistical analyses were performed using SPSS v.16. For categorical measures, Fisher's exact test or Pearson's chi-square test was used; for continuous measures, unpaired Student's t test was used.

Results

Clinical characteristics

From October to December 2009, 113 confirmed patients with 2009 influenza A(H1N1) virus infection were hospitalized in our clinic and included in the study. The ages of the patients were between 17 and 77 years (mean age 35.7 ± 15.8 years) and 73 (64.6%) were female. Cough (92.9%), fever (85.8%), malaise

(85.8%), headache (80.5%), and muscle aches (85.0%) were the most common presenting symptoms. The time from symptom onset to hospital admission was 1-15 days (mean time 3.8 ± 3 days) (Table 1). Twenty-five patients (22.1%) had a history of contact with 2009 influenza A(H1N1) virus infected persons. None of the 113 patients had received swine flu vaccine.

On physical examination, fever (74.3%), pharyngeal hyperemia (66.4%), rales (43.4%), dyspnea (29.2%), and cyanosis (4.4%) were the presenting clinical findings (Table 2). Of the 113 hospitalized patients, 64 (56.6%) had at least 1 underlying medical condition and 15 (13.3%) had 2 such conditions. The most common underlying disease was chronic pulmonary disease (14.5%). It was followed by diabetes mellitus (Table 3). A total of 25 patients were pregnant, of whom 4 had an underlying diseases (asthma in 1 patient, hypothyroidism in 2 patients, and diabetes mellitus in 1 patient).

Table 1. Demographic characteristics and symptoms of hospitalized patients with confirmed 2009 influenza A(H1N1) virus infection.

Characteristics	No. (%) of Patients (n = 113)
Age, years	
Mean age	35.7 ± 15.8 (17-77)
Age \leq 40 years	75 (66.4)
Age $>$ 40 years	38 (33.6)
Female gender	73 (64.6)
Contact with H1N1 infected patient	25 (22.1)
Time from onset to admission, days	3.8 ± 3 (1-15)
Cough	105 (92.9)
Fever	97 (85.8)
Malaise	97 (85.8)
Muscle aches	96 (85.0)
Headache	91 (80.5)
Sore throat	75 (66.4)
Nausea	66 (58.4)
Shortness of breath	59 (52.2)
Chills	53 (46.9)
Rhinorrhea	33 (29.2)
Vomiting	30 (26.5)
Diarrhea	10 (8.8)

Table 2. Clinical and laboratory findings of hospitalized patients with confirmed 2009 influenza A(H1N1) virus infection.

Characteristics	No. (%) of Patients (n = 113)
Fever	84 (74.3)
Pharyngeal hyperemia	75 (66.4)
Rales on chest examination	49 (43.4)
Dyspnea	33 (29.2)
Cyanosis	5 (4.4)
Leukopenia (WBC ^a < 4400/mm ³)	25 (22.1)
Leukocytosis (WBC > 11,300/mm ³)	12 (10.6)
Neutrophilia (neutrophils > 74%)	54 (47.8)
Neutropenia (neutrophils < 45%)	11 (9.7)
Lymphocytosis (lymphocytes > 45%)	6 (5.3)
Lymphopenia (lymphocytes < 18%)	60 (53.1)
Monocytosis (monocytes > 13%)	16 (14.2)
Thrombocytopenia (thrombocytes < 150,000/mm ³)	29 (25.7)
Elevation of ALT/AST ^b (>45 U/L)	26 (23.0)
Elevation of creatinine (>1.4 mg/dL)	6 (5.3)
Hyperglycemias (>115 mg/dL)	25 (22.1)
Hypoxia ^c SO ₂ < 90% SO ₂ < 80%	24 (21.2) 13 (11.5)
Infiltration on chest radiography	47 (41.6)

Abbreviations: WBC^a: White blood cell, ALT/AST^b: Alanine aminotransferase/Aspartate aminotransferase, ^cSO₂: Oxygen saturation

Laboratory findings

On admission to hospital, 76 patients (67.3%) had white blood cell (WBC) counts in normal ranges, 25 patients (22.1%) had leukopenia, 12 patients (10.6%) had leukocytosis, and 29 patients (25.7%) had thrombocytopenia. Leukocyte formulas revealed neutrophilia in 47.7% and lymphopenia in 53.1% of the patients. Biochemical test results showed hyperglycemias (5.3%), and elevated ALT/AST (23%) and creatinine (5.3%) levels. Pulmonary infiltrates consistent with pneumonia were detected on chest radiography in 47 (41.6%) patients. Oxygen saturation was below 90% in 24 patients (21.2%) (Table 2). All culture results (blood, sputum, urine etc.) were negative.

Table 3. Underlying medical conditions of hospitalized patients with confirmed 2009 influenza A(H1N1) virus infection.

Underlying Medical Conditions	No. (%) of Patients (n = 113)
Pregnancy ^a	25 (34.2)
Obesity ^b	2 (1.8)
Chronic pulmonary disease ^c	17 (14.5)
Diabetes mellitus	13 (11.5)
Hypertension	13 (11.5)
Cardiovascular disease ^d	6 (5.1)
Malignancy	4 (3.5)
Hypothyroidism	4 (3.5)
Others	3 (2.7)
Total	64 (56.6)

^aThe ratio was calculated between the female patients.

^bMean body mass index greater than 30.

^cIncluding asthma and COPD.

^dIncluding ischemic heart disease, congestive heart failure, and arrhythmia.

Treatment

Of the 113 patients, 98 (86.7%) received oseltamivir treatment on admission (Table 4). Fifteen patients (13.3%) refused to receive oseltamivir because of pregnancy. Oseltamivir treatment was started within 48 h of the onset of symptoms in 45.1% of the patients. The other patients received oseltamivir after 48 h from the onset of symptoms because of late admission to the hospital. In 73 patients (64.6%), antibiotic treatment was initiated empirically. Of these patients, 47 had pulmonary infiltrates on chest radiography and the other 26 had symptoms of acute sinusitis or COPD. Commonly used antibiotics included beta-lactams, quinolones, and macrolides.

Outcome

Six patients (5.3%) were admitted to the ICU because of acute respiratory failure and 4 of them (3.5%) required mechanical ventilation. All these 6 patients were younger than 40 years old. Their laboratory test results revealed leukopenia in 4 patients, thrombocytopenia in 3, hyperglycemias in 5, elevated ALT/AST levels in 4, and elevated creatinine levels in 2. The time from onset of symptoms to

Table 4. Treatment and outcome of hospitalized patients with confirmed 2009 influenza A(H1N1) virus infection.

Treatment and Outcome	No. (%) of Patients (n = 113)
Oseltamivir treatment	98 (86.7)
Oseltamivir treatment received within 48 h of onset of symptoms	51 (45.1)
Antibiotic treatment	73 (64.6)
Intensive care unit admission	6 (5.3)
Required mechanical ventilation	4 (3.5)
Fatal cases	3 (2.7)
Median duration of hospitalization, days	2 (1-27)

hospital admission was longer than 3 days in all of them. An underlying medical condition was detected in 2 patients (pregnancy and COPD). All of these 6 patients received oseltamivir and antibiotic treatment. Only 1 patient received oseltamivir within 48 h of the onset of symptoms.

Among 113 hospitalized patients with 2009 influenza A(H1N1) virus infection, 3 patients (2.7%) died in the ICU. The patients died 6, 8, and 41 days after the onset of illness. The time periods between the ICU admissions to death were 2, 4, and 27 days. The dead patients were younger than 40 years old (19, 27, and 39 years). None of them had an underlying medical condition. All 3 patients who died had thrombocytopenia, severe hypoxemia, and pulmonary infiltrates on chest radiography on admission. Two of them had leukopenia; their WBC counts were 1300/mm³ and 1100/mm³. These non-surviving patients developed ARDS and disseminated intravascular coagulation (DIC) during their ICU stay. All of the patients who died received oseltamivir and antibiotics. None of them received oseltamivir within 48 h of the onset of symptoms because of late admission to hospital.

The surviving patients (110, 97.3%) were discharged without any complication. The mean duration of hospitalization for the surviving patients was 2.9 ± 2.1 days.

Analysis of patients with pneumonia:

A comparison between the patients with and without pneumonia was performed statistically (Table 5). Age older than 40 years old, time from onset of symptoms to admission longer than 3 days, leukocytosis, ALT/AST elevation, and hyperglycemia were significantly higher in patients with pneumonia.

Discussion

The age distribution of incidence of H1N1 influenza is different from that of seasonal influenza. Young adults were the most affected people. Although underlying medical conditions were common in the hospitalized patients, severe illness was identified among the young, healthy persons (6,8,9). In our analysis, most of the patients, including those admitted to the ICU, were under 40 years old. Other reports with a large number of patients suggested that although young people were the most affected, mortality was higher in older ages (6-8,10).

Signs and symptoms of 2009 influenza A (H1N1) virus infection are similar to those of seasonal influenza. As reported in this paper, the typical symptoms are fever, cough, sore throat, rhinorrhea, myalgia, headache, and fatigue. Vomiting and diarrhea were detected more commonly than in seasonal influenza (6,7,10). In our series, vomiting was reported in 26.5% of the patients, with diarrhea in 8.8%.

In a pattern similar to that of seasonal influenza, a large number of the hospitalized patients with H1N1 influenza had underlying medical conditions, and chronic pulmonary diseases were the most common condition (5,6,8,9). In this report, underlying medical conditions were present in 56.6% of the patients, with chronic pulmonary diseases ranking first (14.5%). Pregnant women were the other important risk group for severe H1N1 influenza (6-8,11,12). In this case series, 25 of the patients were pregnant and 1 of them was followed up in the ICU.

Our series showed that the pandemic H1N1 infection resulted in ICU admission in 5.3% of hospitalized patients and death in 2.7%. A report from the US suggested higher rates, stating that, from 272 hospitalized patients, 25% were admitted to the ICU and 7% died. In that series, 45% percent of the

Table 5. Comparison of patients with and without pneumonia.

Characteristics	No. (%) of Patients		P value
	with pneumonia (n = 47)	without pneumonia (n = 65)	
Mean age	41.9 ± 17.1	31 ± 13.4	<0.001
Age > 40 years	23 (62.2)	14 (37.8)	0.004
Female gender	26 (36.1)	46 (63.9)	0.112
Underlying medical conditions	31 (49.2)	32 (50.8)	0.086
Time from symptom onset to admission	5.1 ± 3.8	2.9 ± 1.9	0.001
Time from onset to admission > 3 days	27 (54)	23 (46)	0.023
Leukopenia (WBC < 4400/mm ³)	13 (52)	12 (48)	0.261
Leukocytosis (WBC > 11,300/mm ³)	9 (75)	3 (25)	0.027
Neutrophilia (>74%)	25 (47.2)	28 (52.8)	0.340
Lymphocytosis (>45%)	3 (50)	3 (50)	0.697
Thrombocytopenia (<150,000/mm ³)	10 (65.5)	19 (34.5)	0.385
Elevation of ALT/AST (>45 U/L)	17 (65.4)	9 (34.6)	0.006
Elevation of creatinine (>1.4 mg/dL)	4 (66.7)	2 (33.3)	0.398
Hyperglycemia (>115 mg/dL)	17 (70.8)	7 (29.2)	0.003
Oseltamivir < 48 h after symptom onset	20 (40)	30 (60)	0.847

patients were under the age of 18 years and 73% had at least 1 underlying medical condition (6).

Pulmonary infection is the most frequent and severe complication of influenza. On admission to our hospital, all the patients underwent chest radiography. Pulmonary infiltrates consistent with pneumonia were detected in 41.6% of the patients. Similarly, other series reported pulmonary infiltrates in the majority of patients. The US series reported pulmonary infection in 40% of hospitalized patients (6). In the Australia and New Zealand series, viral pneumonia or ARDS developed in 48.8% of critically ill patients and secondary bacterial pneumonia in 20.3% (13).

Patients who were admitted to the ICU and who died had shortness of breath, and radiographically shown pneumonia and hypoxia. During ICU stay, ARDS developed in the fatal cases. The other reports also stated that patients who were admitted to the ICU and who died were more likely to have pneumonia and respiratory failure (7,6,9). Thus it can be concluded that pulmonary status of the patient is an important clue for the prognosis of H1N1 influenza.

While we detected WBC counts in the normal range in most of the patients, neutrophilia and lymphopenia were found in the majority. This is an interesting finding. Lymphocytosis was expected in a viral disease. Thrombocytopenia was another important characteristic of the disease. In the US case series, 20% of patients had leukopenia, 18% had leukocytosis, and 14% had thrombocytopenia, which is similar to our results (6).

Among the ICU-admitted 6 patients, 4 had leukopenia and 3 had thrombocytopenia. Moreover, all patients who died had thrombocytopenia and 2 had leukopenia. The numbers of these patients are too small for a statistical comparison, but it seems that leukopenia and thrombocytopenia are common in severe cases. Thus, we considered that leukopenia and thrombocytopenia might have a prognostic value for 2009 influenza A (H1N1) infection.

We recommended antiviral treatment to all of the patients on admission, including pregnant women, as the CDC states (14). All the patients who were not pregnant received antiviral treatment. Interestingly,

more than half of the pregnant women did not accept the antiviral treatment, although the risk of infection in pregnancy and the safety of the drug for the fetus were explained to them.

Data suggest that early antiviral treatment is important for prognosis of the disease. In our series none of the patients who died received oseltamivir within 48 h of the onset of symptom and only 1 patient admitted to the ICU was started on early treatment. In the US series none of the 19 non-surviving patients received antiviral treatment within 48 h of the onset of symptoms (6). Delayed initiation of antiviral treatment may contribute to an increased severity of illness.

Blood cultures were done in the patients with leukocytosis or pulmonary infiltration on chest radiography. However, all the blood cultures were negative. Thus, bacterial co-infections were not detected in any patients. Some patients received antibiotics before the culture collection, which could have reduced the diagnostic sensitivity. Microbiologic evidence of secondary bacterial infection is also uncommon in other series. In the US series, only 3 of 182 patients had positive blood cultures (6). *E. coli* (urosepsis), *S. pneumoniae* (pneumonia), and *S. aureus* (pneumonia) were the growth bacteria. In the California series, secondary bacterial infection was identified in 4% of patients (7).

All the patients with pulmonary infiltration on chest radiography received antibiotics. The same approach is common in the literature. In other series, 97%-98.8% of the patients with pulmonary

infiltration were given broad spectrum antibacterial agents because of initial suspicion of bacterial pneumonia (6,8). We could not confirm secondary bacterial pneumonia with laboratory tests but we considered the possibility of secondary bacterial pneumonia clinically in the patients with pulmonary infiltration and initiated antibiotic treatment empirically. The risk of this approach is improper use of antibiotics. However, it is reported that, in the absence of accurate diagnostic methods, patients who are hospitalized with suspected influenza and pulmonary infiltrates on chest radiography should be considered for treatment with both antibiotics and antiviral drugs (6).

Age older than 40 years old, late admission, leukocytosis, ALT/AST elevation, and hyperglycemia were significantly more common in patients with pneumonia. A higher rate of complications in older patients is an expected finding. Hyperglycemia is a known risk factor for complications and death. Delayed admission was also associated with increased risk of severity in other series. In a previous report, the risk increased 1.19-fold per day (5). Leukocytosis may be related to secondary pulmonary infection.

In conclusion, although the 2009 influenza A(H1N1) virus causes severe illness including pneumonia and death, the mortality rate is not very high. The characteristics of the disease are similar to those of seasonal influenza. Young adults were the most affected persons and most of the patients had underlying medical conditions.

References

1. Centers for Disease Control and Prevention (CDC). Update: novel influenza A (H1N1) virus infections worldwide. May 6, 2009. MMWR. Morb Mortal Wkly Rep May 8, 2009; 58: 453-58.
2. World Health Organization. Pandemic (H1N1) 2009. Update 58, 6 July 2009. Available from: http://www.who.int/csr/don/2009_07_06/en/index.html. Accessed August 15, 2009.
3. Chan M. World now at the start of 2009 influenza pandemic. Available from: http://www.who.int/mediacentre/news/statements/2009/h1n1_pandemic_phase6_20090611/en/index.html. World Health Organization. Accessed August 15, 2009.
4. Novel Swine-Origin influenza A (H1N1) Virus Investigation Team. Emergence of a novel swine-origin influenza A (H1N1) virus in humans. N Engl J Med 2009; 360: 2605-15.
5. 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: 2072-9.
6. 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: 1935-44.

7. 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: 1896-902.
8. 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: 1872-9.
9. Domínguez-Cherit G, Lapinsky SE, Macias AE, Pinto R, Epinosa-Perez L, de la Torre A et al. Critically Ill patients with 2009 influenza A(H1N1) in Mexico. *JAMA* 2009; 302: 1880-7.
10. Satpathy HK, Lindsay M, Kawwass JF. Novel H1N1 virus infection and pregnancy. *Postgrad Med.* 2009; 121: 106-12.
11. Oliveira W, Carmo E, Penna G, Kuchenbecker R, Santos H, Araujo W et al. Pandemic H1N1 influenza in Brazil: analysis of the first 34,506 notified cases of influenza-like illness with severe acute respiratory infection (SARI). *Euro Surveill.* 2009; 14: 19362. Erratum in: *Euro Surveill.* 2009; 14(43).
12. 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: 1925-34.
13. 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: 1925-34.
14. Centers for Disease Control and Prevention (CDC). Updated interim recommendations for the use of antiviral medications in the treatment and prevention of influenza for the 2009-2010 season. Available from: <http://www.cdc.gov/H1N1flu/recommendations.htm>