

*Original Article***Clinical features of novel 2009 influenza A (H1N1) infection in Isfahan, Iran**

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Abstract

BACKGROUND: During August 2009, novel H1N1 influenza virus began causing illness in Isfahan. Since rates of hospitalization and mortality due to the disease have varied widely in different countries, we described the clinical, radiologic, and demographic features of H1N1 hospitalized patients in a hospital in Isfahan.

METHODS: This cross-sectional study was conducted in Alzahra Hospital during September 2009 to February 2010. Totally, 216 patients with confirmed, probable, or suspected cases of 2009 influenza A (H1N1) were admitted.

RESULTS: Most patients were women (50.5%). Mean age of patients was 26.6 ± 19.5 years. The most common complaints on admission were respiratory symptoms (91.6%, n= 198), fever (88.4%, n = 191), myalgia (65.7%, n = 142). In addition, 120 patients (56%) had at least one underlying medical disorder. Thirty-six patients (16.7%) died. Mortality was higher in children under 5 years old (10/36, 10%) and female cases (63.9% of died patients). Predicting variables affecting mortality were intensive care unit (ICU) admission and procalcitonin (PCT) > 0.5. Antiviral treatment was prescribed for 200 (92.5%) of the 216 patients.

CONCLUSIONS: Based on the findings of the present study, novel H1N1 influenza is highly prevalent among the youth. Moreover, it causes a relatively high morbidity rate. Therefore, people need to be encouraged to have vaccination against 2009 H1N1. Early diagnosis and treatment is related to less admission and shorter duration of hospitalization.

KEYWORDS: Novel H1N1, Clinical Manifestations, Demographic Features.

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Influenza virus has caused recurrent epidemics of febrile respiratory disease every 1-3 years. Novel 2009 influenza A (H1N1) virus is a new strain of the flu virus and a "quadruple reassortant" resulting in respiratory illness. An outbreak of a novel respiratory infection was identified in late March 2009 and spread rapidly across many countries. Generally, novel influenza has already had two waves, one in late spring 2009 and one in early fall

2009.^{1,2} The first documented 2009 H1N1 flu patient in Isfahan was a pregnant woman with a past medical history of asthma. She had returned from Saudi Arabia in August 2009, approximately 3 months after the first reports of novel influenza A cases in Mexico and the United States.³ During August 2009, novel H1N1 influenza virus began causing illness in Isfahan. Since rates of hospitalization and mortality have varied widely according to coun-

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tries,⁴⁻⁶ we tried to characterize clinical findings and demographic features of hospitalized patients with severe novel influenza A (H1N1) during the second wave in Isfahan.

Methods

After arrival of the H1N1 virus infection to Isfahan, the Infectious Diseases and Tropical Medicine Research Center of Isfahan University of Medical Sciences decided to evaluate the clinical features and radiologic findings of the disease. We hereby cover the clinical part of the mentioned research.

This was a cross-sectional study conducted in Alzahra Hospital, Isfahan during September 2009 to February 2010. According to a chart review, all patients admitted in Alzahra Hospital with a diagnosis of H1N1 influenza A were studied. Confirmed cases of H1N1 were documented by reverse transcriptase-polymerase chain reaction (RT-PCR). Charts of admitted patients were reviewed for epidemiologic and clinical data. All of 216 confirmed, probable, or suspected 2009 influenza A (H1N1) patients were studied. The data including demographic and clinical findings were collected by a special questionnaire and finally analyzed by SPSS₁₈. Chi-square and student's *t* tests were used for data analysis. Logistic regression analysis was employed to determine the risk factors for mortality.

Results

A total of 216 patients, including 107 (49.5%) males and 109 females (50.5%), were admitted to our center since September 2009 to February 2010. Male to female ratio was equal. The mean age was 26.6 ± 19.5 . Mean hospital stay was 9.08 ± 6.62 days (range = 1-35 days). In addition, length of hospitalization for patients admitted in intensive care unit (ICU) was 13.1 ± 6.4 days (range = 2-35 days). None of our cases had history of H1N1 vaccination.

Most patients were admitted in October and November (48.6% and 41.7%, respectively). Moreover, 61 (28.2%) patients aged less than 16 years and 10 (4.6%) were pregnant. Underlying medical conditions were seen in 121 (56%) pa-

tients. The most common underlying medical conditions were respiratory diseases (including asthma, chronic obstructive pulmonary (COPD) and allergy) and diabetes mellitus [52 (24.1%) and 23 (10.6%) patients, respectively].

Diagnosis was confirmed mostly within the first 5 days of symptoms onset. The mean \pm SD of time from symptoms onset to hospitalization was 4.99 ± 3.05 days (range: 1-15 days). The time between symptoms onset and admission was significantly related with the length of hospital stay ($p = 0.002$)

Unfortunately, 36 patients (16.7%) died from which 13 (36.1%) were male and 23 (63.9%) were female. However, no statistically significant relation was seen between death and sex according to chi-square test ($p = 0.08$).

The mean \pm SD of age for patients who died and stayed alive was 24.3 ± 22.8 and 27 ± 18.8 years, respectively ($p = 0.44$).

Of 216 hospitalized patients, 54 (31.2%) were admitted in the ICU and 51 (94%) required mechanical ventilation. The mean age of admitted patients in the ICU was 26.3 ± 22.5 years and the mean age of other patients was 25.3 ± 19.2 ($p = 0.77$). Mortality rate in the ICU was 63% (34 patients). There was not any obvious underlying disease in 36.1% of the dead patients, but 13.9% had respiratory abnormalities (e.g. asthma, COPD, allergy) and 11.1% were diabetic cases.

The median pulse rate was 96 beats/min (range: 70-150). Age-specific normal range showed that 57 patients (36.3%) had tachycardia and 15 patients (17.6%) had severe tachypnea (respiratory rate > 30). Fever was seen in 191 patients (88.4%) (median: 38.1°C , range: 36-40).

The median oxygen saturation level ($\text{O}_2\text{-sat}$) and partial pressure of CO_2 (pCO_2) were 90% and 30 mmHg, respectively. 61 patients (28%) had lymphopenia (< 1000 lymphocytes per cubic millimeter). The mean number of platelets and white blood cells (WBC) were 192090 ± 115764.4 and 10777 ± 12307 , respectively. The mean value of hemoglobin, erythrocyte sedimentation rate (ESR), and blood pH were 11.96 ± 2.76 g/dl, 39.9 ± 36.2 mm/hour, and 7.33 ± 0.10 , respectively.

Of the 110 patients who had chest radiographs, 61 (55%) had abnormalities suggestive of pneumonia. Radiologic abnormalities are summarized in table 1.

Antiviral drug (oseltamivir) was prescribed

for 48 patients (94.1%) and 49 patients (90.7%) received antibiotics to treat superinfections. Logistic regression method showed that ICU admission and procalcitonin level were risk factors for predicting mortality ($p < 0.05$) (Table 2).

Table 1. Frequency distribution of radiologic abnormalities among hospitalized H1N1 infected patients during the second wave of pandemic flu in Isfahan, Iran, 2009

Findings	Percent
Normal	45.5
Patchy infiltration	13.6
Interstitial infiltration	25.5
Pleural effusion	4.5
Pleural effusion with infiltration	10.9
Unilateral involvement	13.6
Bilateral involvement	40.9
Upper lobe involvement	1.8
Middle lobe involvement	12.7
Lower lobe involvement	26.4
Middle and lower lobe involvement	11.8

Table 2. Multivariate logistic regression model of death

Variable	Adjusted OR* (95% CI)	Non-adjusted OR* (95% CI)	p
Sex ^a	9.24 (0.7-120.6)	1.93 (0.92-4.05)	0.10
Age	0.99(0.93-1.04)	0.99 (0.97-1.01)	0.80
Malignancy	0.99 (0.014-70.9)	1.8 (0.33-9.6)	0.10
Diabetes mellitus	1.16 (0.095-14.37)	1.3 (0.38-4.5)	0.90
Pregnancy	0.2 (0.002-23)	0.7 (0.08-6)	0.50
Obesity	54.6 (0.9-3307.6)	6.3 (1.14-34.6)*	0.06
Respiratory diseases	0.06 (0.003-1.14)	0.67 (0.22-2)	0.06
Immunodeficiency	0.026 (0.001-1.01)*	1.8 (0.33-9.6)	0.05
Hemoglobinopathy	0.81 (0.0-1957.5)	3.15 (0.26-37.3)	0.10
Renal Hemodialysis	19.9 (0.000-E)	9.4 (1.4-62)*	0.80
Tamiflu ^c	19.08 (0.61-588)	1.46 (0.36-5.8)	0.10
Procalcitonin ^d	84.1 (5.6-1263.9)*	58 (13-259)*	0.001
ICU admission ^b	224.9 (13.44-3760.9)*	104.5 (23-469)*	< 0.001

* Significant at the 0.05 level

OR: Odds ratio; a = reference category = Male; c = reference category = received; d = reference category = PCT < 0.5.

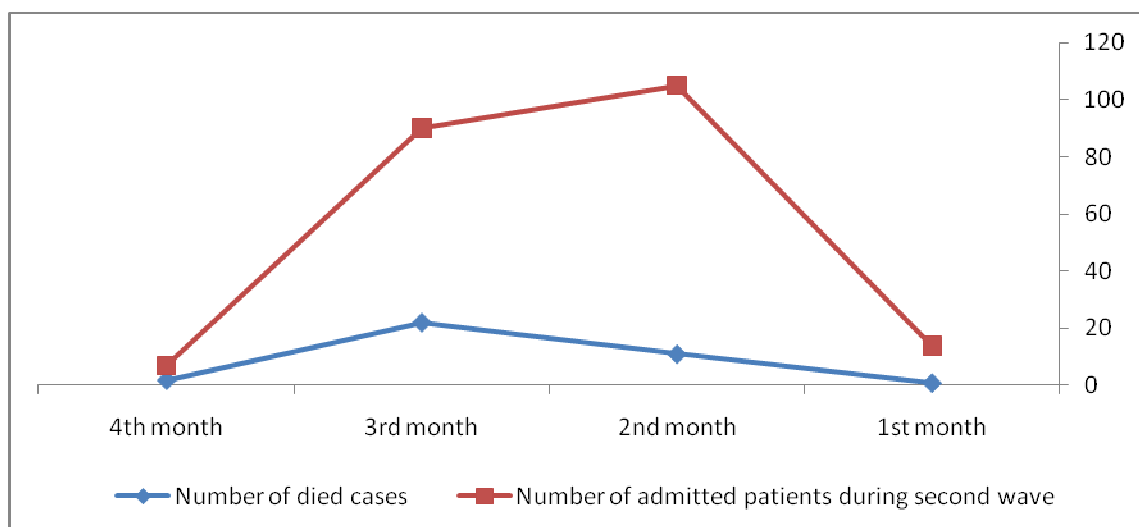


Figure 1. Number of admitted patients compared to deceased cases (from 23th September 2009, during the second wave of H1N1 influenza in Alzahra Hospital, Isfahan, Iran, 2009).

Discussion

The aim of this study was to understand the epidemiological and clinical aspects of H1N1 infected patients admitted in Alzahra Hospital.

Morbidity and mortality rates varied widely according to various part of the country.⁷ The novel H1N1 virus caused complications, including pneumonia and septic shock, and resulted in ICU admissions in 9-31% of patients and death in 14-46%.^{6,7} According to Gooya and Soroush, geographic distribution of the reported H1N1 cases showed the highest rates in central and eastern provinces of Iran.¹ This is the first report to summarize the epidemiology of 2009 H1N1 in Isfahan (a province in central Iran). The first case was a pilgrim pregnant woman.

At initial assessment, the most common findings were respiratory signs (including cough, sore throat, rhinorrhea) (164/216; 75.9%), fever (191/216; 88.4%) and myalgia (142/216; 65.7%). Gooya and Soroush reported 61.5% and 48.9% of patients to have a history of fever and myalgia, respectively. In addition, cough was the first complaint in 56% of patients.¹ In our study, respiratory symptoms were the most common symptoms before admission. Among 268 patients in the United States, clinical findings included fever (93%), cough (83%), shortness of breath (54%), fatigue or weakness (40%), chills (37%), myalgia (36%),

rhinorrhea (36%), sore throat (31%), headache (31%), vomiting (29%), wheezing (24%), and diarrhea (24%).⁸ Dominguez-Cherit et al. found body mass index (BMI) as a major risk factor of death.⁹

In the first report of confirmed cases of H1N1 from Iran, Gooya and Soroush suggested that the mean age of deceased patients was 26.5 ± 20.6 years. Approximately 80% of patients aged less than 40 years. Similar to our study, they did not find significant correlations between the prevalence of death and sex and age ($p = 0.321$ and 0.052 , respectively).¹ We also found that age had no significance correlation with the time seeking for medical care before hospitalization and the length of hospital stay ($p = 0.59$ and 0.48 , respectively). However, the time between symptoms onset and admission had a significant positive relationship with length of hospital stay ($p = 0.002$).

In our study, mortality rate was 16.7% in hospitalized patients and 63% in ICU-admitted patients. Donaldson et al.¹⁰ and Schout et al.¹¹ reported the mortality rate of novel influenza A (H1N1) virus to be 28.1% and 30.2%, respectively. Among patients with 2009 H1N1 virus infection, pregnant women accounted for up to 7-10% of hospitalized patients,⁴ 6-9% of ICU patients, and 6-10% of patients who died.⁷ While we found that 2 (3.7%) of ICU patients were pregnant women, some studies reported

rates as high as 6-9%.^{5,7} Gooya and Soroush reported no mortality in pregnant women.¹

Among chest radiography of 110 hospitalized patients, 50 (45.5%) had normal radiography. In this study the most common abnormal radiologic finding of lung was bilateral interstitial infiltration, predominantly in lower lobes.

Similar to Lee et al.,¹² 70 patients (15.4%) had pleural effusion. It has been shown that peak of mortality lags roughly 2 weeks behind the peak of influenza activity.¹³ This is possibly the result of several different time delays from different influenza mortality pathways.¹⁴ Admission and mortality curves are shown in figure 1.

Conflict of Interests

Authors have no conflict of interests.

Authors' Contributions

AAJ, BA, AB, MR, KM, MM, AE, HS, MA, RS, MRY, and FR planned the study, collected specimen and supervised the project in cooperation with FK. FK and FR prepared the first draft of the manuscript. AB performed statistical analysis and prepared the first draft of the manuscript. FK, AAJ, MR, MA, MRY and FR prepared the final version the manuscript

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