

Characteristics and outcome of critically ill patients with 2009 H1N1 influenza infection in Syria

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ABSTRACT

Objectives: To describe the epidemiologic characteristics, clinical features, and outcome of severe cases of 2009 H1N1 influenza A infections who were admitted to the intensive care units (ICUs) in Damascus, Syria. **Materials and Methods:** Retrospectively, we collected clinical data on all patients who were admitted to the ICU with confirmed or suspected diagnosis of severe 2009 H1N1 influenza A with respiratory failure at 4 major tertiary care hospitals in Damascus, Syria. Acute Physiology and Chronic Health Evaluation (APACHE) II system was used to assess the severity of illness within the first 24 h after admission. The outcome was overall hospital mortality. **Results:** Eighty patients were admitted to the ICU with severe 2009 H1N1 infection. The mean age was 40.7 years; 69.8% of patients had ≥ 1 of the risk factors: asthmatics 20%, obesity 23.8%, and pregnancy 5%; and 72.5% had acute lung injury or adult respiratory distress syndrome, 12.5% had viral pneumonia, 42.5% had secondary bacterial pneumonia, and 15% had exacerbation of airflow disease. Mechanical ventilation was required in 73.7% of cases. The mean hospital length of stay was 11.7 days (median 8 days, range 0–77 days, IQR: 5–14 days). The overall mortality rate was 51% for a mean APACHE II score of 15.2 with a predicted mortality of 21% (standardized mortality ratio of 2.4, 95% confidence interval: 1.7–3.2, P value < 0.001). **Conclusion:** Critically ill patients with severe 2009 H1N1 infection in this limited resource country had a much higher mortality rate than the predicted APACHE II mortality rate or when compared with the reported mortality rates for severe cases in other countries during 2009 H1N1 pandemic.

Keywords: Adult respiratory distress syndrome, H1N1, pandemic, Syria

INTRODUCTION

In April 2009, the Mexican Secretariat of Health reported an outbreak of respiratory disease. In the affected patients, a novel swine origin influenza A (H1N1) virus (S-OIV) with molecular features of North American and Eurasian swine, avian, and human influenza viruses^[1-4] was found. In the same month, the World Health Organization (WHO) classified the global spread of this virus as a public health event of international concern. After documentation of human to human transmission of the virus in at least 3 countries of 2 WHO regions, the WHO raised the pandemic level to 6.^[5]

The first case of 2009 H1N1 Influenza A infection was reported in Damascus, Syria, on August 23, 2009. The greatest burden of H1N1-related critical illness and death occurred in Syria between July 1, 2009, and February 28, 2010. The objective of this study was to describe the epidemiologic characteristics, clinical features, and outcome of severe cases of 2009 H1N1 influenza A patients who were admitted to the intensive care units (ICUs) in Damascus.

This study was presented as an Abstract (poster) at the 40th critical care congress of the Society of Critical Care Medicine in San Diego, California, in February 2011.

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MATERIALS AND METHODS

We performed a multicenter inception-cohort study involving 4 ICUs in 4 main university and ministry of health hospitals in Damascus, Syria (Al-Mouassat Hospital, Damascus Hospital, Assad University Hospital, and Ibn Alnafees Hospital) under the supervision of the regional office of the WHO in Syria. From July 1, 2009, to February 28, 2010, we identified all patients admitted to the ICU with suspected or confirmed infection with the 2009 pandemic influenza A (H1N1) virus. The 2009 H1N1 influenza was confirmed by means of a polymerase chain reaction (PCR) assay or serologic analysis. The PCR assay was conducted initially at reference laboratories in each region and later, as the pandemic evolved, at local laboratories.

We collected the following data on these patients: dates of admission to the hospital and the ICU, age, sex, pregnancy coexisting conditions, body mass index (BMI), date of first symptoms; presence and type of influenza syndrome, including viral pneumonitis or the acute respiratory distress syndrome, secondary bacterial pneumonia, exacerbation of airflow limitation due to either asthma or chronic obstructive pulmonary disease, or intercurrent illness; and the need for mechanical ventilation. We categorized patients according to the age groups used in a previous report^[6]: 5–24 years, 25–49 years, 50–64 years, and 65 years or older. Acute Physiology and Chronic Health Evaluation (APACHE) II system was used to assess the severity of illness within the first 24 h after admission to the ICU. The outcome was overall hospital mortality.

RESULTS

We identified 80 patients with influenza A infection who were admitted to ICU between July 1 and February 28, 2010, distribution of admission per week of the year during the

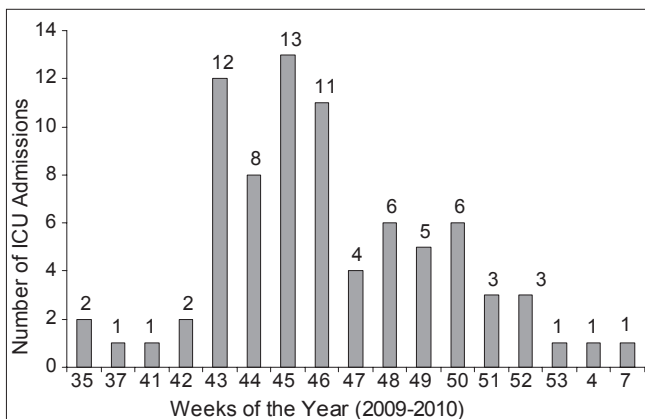


Figure 1: Epidemic curve of intensive care unit admitted cases of the pandemic 2009 influenza A (H1N1) virus reported in Damascus, Syria

pandemic wave is depicted in Figure 1. Of these, 56 (70%) had a confirmed infection with 2009 pandemic influenza A (H1N1) virus. The 2009 H1N1 virus was diagnosed by means of PCR assay in 54 patients and serologic analysis in 2 patients. Twenty-four patients had probable diagnosis with typical presentation of whom the tests were negative.

The number of admissions varied substantially according to the age group. The highest number of ICU admissions was among patients 25–49 years of age [Figure 2].

Additional demographic data and data on risk factors and type of critical illness among patients with 2009 H1N1 influenza are presented in Table 1.

A total of 4 of the 80 patients (5%) admitted to the ICU with 2009 H1N1 influenza were pregnant women, 19 patients (23.8%) had BMI > 30, 16 (20%) had asthma or another chronic pulmonary disease, 6 (7.5%) had chronic cardiovascular disease, and 25 (30.2%) had no predisposing factors. Median APACHE II score was 15 with interquartile range (IQR) of 12–18, and a median SOFA score was 5 and IQR of 3–7.

Median duration from start of symptoms till hospital admission was 3 days with IQR of 3–5 days. Fever was present in 100% of all patients, cough in 95%, and shortness of breath in 86%, additional presenting symptoms and their percentage are presented in Table 2

Creatinine phosphokinase was elevated in 36 patients (45%), lactate dehydrogenase was more than 450 IU/Liter in 41 patients (51.3%), and erythrocyte sedimentation rate was elevated in 34/47 patients (72%), leukocytosis of >12,000 was seen in 23 of 80 patients (28.7%).

Patients were admitted to ICU with the diagnosis of respiratory failure in 86.2%, 58 patients (72.5%) had

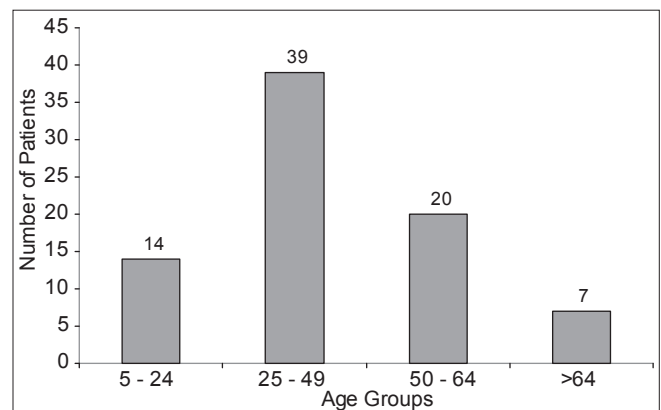


Figure 2: Number of admissions to the intensive care unit, according to age group

acute lung injury or adult respiratory distress syndrome, 10 patients (12.5%) had viral pneumonia, 34 patients (42.5%) had secondary bacterial pneumonia (ie, unilateral or bilateral asymmetric lung infiltrates consistent with bacterial pneumonia, with proven or suspected bacterial infection), and 12 patients (15%) had exacerbation of airflow disease, such as asthma or COPD [Figure 3].

Mechanical ventilation was required in 59 patients (73.7%) for an average duration of 10.6 days (median 10 days, range 1–36 days, IQR 2–18 days), 47 out of 59 patients (79.7%) were placed on muscle paralysis during their stay on mechanical ventilation.

Table 1: Baseline characteristics of patients with confirmed critical illness related to the 2009 H1N1 influenza

Characteristics	Value
Age (yr)	
Median	40
IQR	27–52
Female sex—no./total no. (%)	32/80 (40)
Pregnant—no./total no. (%)	4/80 (5)
Adults with BMI > 30—no./total no. (%)	19/80 (23.8)
Diabetes—no./total no. (%)	21/80 (26.3)
Asthma or chronic pulmonary disease—no./total no. (%)	16/80 (20)
Chronic cardiovascular disease—no./total no. (%)	6/80 (7.5)
No known predisposing factors—no./total no. (%)	25/80 (30.2)
Time from first symptoms to hospital admission—days	
Median	3
IQR	3–5
Influenza syndrome—no./total no. (%)	
Respiratory failure	69/80 (86.3%)
ALI or ARDS	58/80 (72.5)
Viral pneumonitis	10/80 (12.5)
Secondary bacterial pneumonia	34/80 (42.5)
Exacerbation of airflow limitation	12/80 (15)
Severity of Illness assessment at ICU admission	
APACHE II: average (IQR)	15 (12–18)
SOFA: median (IQR)	5 (3–7)

ALI, Acute lung injury; ARDS, acute respiratory distress syndrome; APACHE, Acute Physiology and Chronic Health Evaluation; ICU, intensive care unit; IQR, interquartile range; BMI, body mass index; SOFA (Sequential Organ Failure Assessment). BMI is the weight in kilograms divided by the square of the height in meters. Time from first symptoms to hospital admission was known for 72 of the 80 patients.

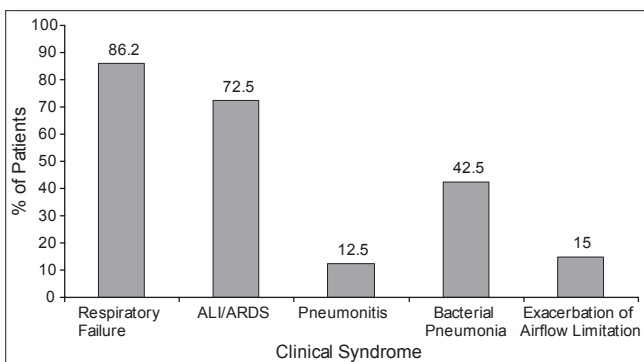


Figure 3: Clinical syndromes on presentation to intensive care unit

Fifty-three patients (66%) were admitted directly to ICU, 27 patients were admitted to the floor and transferred to ICU after deterioration of their condition. Nineteen of these 27 patients (70%) deteriorated within the first 72 h after admission. The mean hospital length of stay was 11.7 days (median 8 days, range 0–77 days, IQR 5–14 days).

The overall mortality rate was 51% for an average APACHE II score of 15.2 with a predicted mortality of 21% (standardized mortality ratio of 2.4, 95% confidence interval: 1.7–3.2, *P*value < 0.001). Mortality was 0% for APACHE II group of 0–9, 54% for 10–19 group, and 67% for the above 20 group [Figure 4].

DISCUSSION

The severe cases of 2009 influenza A (H1N1) infection outbreak in Damascus affected primarily young males conferring a mortality of 51% among critically ill patients compared with 41.4% in Mexico,^[7] 17.3% in Canada,^[8] 14%

Table 2: Presentation symptoms of patients admitted to intensive care unit

Symptoms	n/N (%)
Fever	80/80 (100)
Fatigue/weakness	55/80 (69)
Headache	28/80 (35)
Altered mental status	16/80 (20)
Seizure	5/80 (6)
Conjunctivitis	11/80 (14)
Nasal congestion	20/80 (25)
Rhinorrhea	21/80 (26)
Sneezing	15/80 (19)
Sore throat	42/80 (53)
Cough	75/80 (95)
Sputum production	52/80 (65)
Hemoptysis	16/80 (20)
Shortness of breath	69/80 (86)
Wheezing	16/80 (20)
Chest pain	41/80 (51)
Abdominal pain	19/80 (24)
Diarrhea	13/80 (16)
Vomiting	17/80 (21)
Myalgia	25/80 (31)

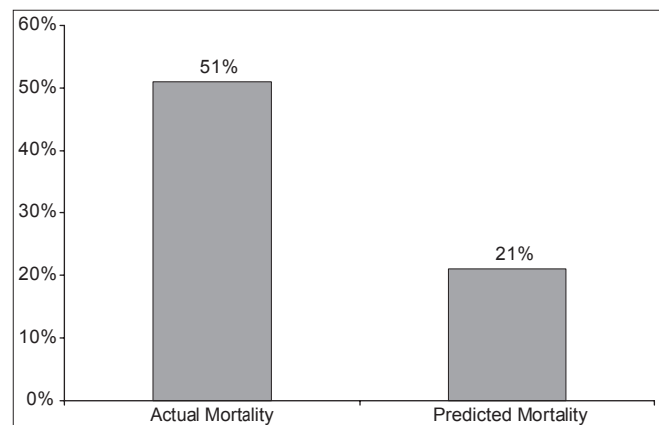


Figure 4: Actual hospital mortality compared with APACHE II predicted mortality

in Australia and New Zealand,^[6] and 28% in the USA.^[9] The age distribution of disease for pandemic 2009 influenza A (H1N1) infection is markedly different from that of seasonal influenza. A history of lung disease, obesity, and cardiovascular disease were the most common comorbidities with almost one third of the patients presented with no predisposing risk factors similar to what has been reported in the literature.^[7-10] Presenting symptoms were more often fever, cough, sore throat, and shortness of breath. While gastrointestinal symptoms are observed infrequently (5%) in adults infected with seasonal influenza, more than one-fourth of adult cases in our series reported at least nausea, vomiting, abdominal pain, or diarrhea. Critical illness occurred rapidly after hospital admission and was associated with severe oxygenation failure, a requirement for prolonged mechanical ventilation, and the frequent use of rescue therapies, including muscle paralysis. The rate of muscle paralysis use of 79.7% is much higher than what is reported in other studies and may in fact give an idea of the local critical care practices in the country. The higher case fatality rate observed in our study cannot be attributed to sicker patients or to a delay in initiating therapies as the average APACHE II score for those patients was 15.2 on admission to ICU compared with the average APACHE II score of 19.7 in the Canadian study^[8] with a mortality rate of 17.3%. It is also much higher than the APACHE II predicted mortality rate of 21% with standardized mortality ratio of 2.4, acceptable 95% confidence interval of 1.7–3.2 and statistical significance with *P* value < 0.001. This high mortality rate should mandate review of the standards of critical care delivery in the country in relation to the structure and designs of critical care units, available equipment, supplies and maintenance, human resources, staff training and ICU management skills, ICU policies, procedures, and different care processes in addition to quality assurance programs.

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