# Clinical and Epidemiological Characteristics of Children With Influenza A H1N1 in Khuzestan, Iran During July 2009–April 2010

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**Background:** Influenza A H1N1 virus had became a world pandemic during June 2009 to July 2010. Children are the most susceptible group to acquire influenza infection and almost half of hospitalized patients are under 18 years of age. On May 10th 2009, The Iranian Ministry of Health launched a system to monitor and report the presence of this new virus throughout the country.
**Objectives:** In this report we summarized the results of surveillance activity in children aged 2-17 years in a southwestern province of Iran, Khuzestan, in response to the emergence of influenza A H1N1 virus during July 2009–April 2010.
**Patients and Methods:** A total of 232 suspected children who fulfilled the case definition criteria were included in this study. Physicians obtained nasopharyngeal swab specimens, and human influenza A H1N1 was detected, using Real time Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) test according to the CDC protocol.
**Results:** Among the 232 enrolled cases, 126 patients (54.31%) were male and 106 patients (45.89%) were female. Real time Reverse RT-PCR test revealed that 18.1% of suspected children were positive for the influenza A H1N1 virus. The most frequent symptoms among the confirmed patients were cough (34, 81%), fever (30, 71%), and myalgia (24, 57%) and five cases (12%) reported diarrhea.
**Conclusions:** Clinical signs and symptoms presented by patients infected with the influenza A H1N1 virus were similar to those described for seasonal influenza, although with more gastrointestinal disorders.

*Keywords:* Influenza A H1N1 virus; Surveillance; Children; Khuzestan

## 1. Background

Human infections of H1N variants of the influenza A virus were first identified in two epidemiologically unrelated patients in the United States in 2009 (1) while shortly after, disease cases were reported from Mexico and Canada (2-4); eventually leading to a pandemic (5-7). The global spread of this pandemic was more rapid than that of the previous pandemics (8). This resulted in the rise of the pandemic alert from level 3 to level 5 within a couple of weeks by WHO (5, 9).

In less than two month, the pandemic alert again increased to its highest level (phase 6) since 1968 (5). After 43 days, WHO declared the beginning of the pandemic peak period (phase VI) on June 11, 2009 (5). The new variant responsible for this serious flu pandemic emerged from a recombination between American and Eurasian swine influenza viruses (2). The first confirmed case of swine flu

in Iran, who was an Iranian traveler from the USA, was reported in June 2009, during this pandemic (8). According to a report by the Iranian Ministry of Health, the number of laboratory-confirmed cases in Iran until November 25th, 2009 was 3672, including 140 deaths.

The manifestation of the disease varies from mild upper to severe lower respiratory tract symptoms capable of leading to a respiratory failure. Symptoms caused by the pandemic influenza A H1N1 virus and the seasonal influenza viruses, such as fever, cough and sneeze, are so similar that their clinical differentiation is very difficult. A significant number of patients, however, demonstrated diarrhea and vomiting, which are unusual in seasonal influenza. In a study conducted in the United States on the H1N1 variant, children and young adults comprised the majority of affected patients so that almost half of the hospitalized patients were under 18 years of age (2). The morbidity of pandemic influenza A H1N1 is high in contrast to its low mortality rates (1-4%) (6). In Iran on May 2009, the Ministry of Health established a procedure to screen and report the existence of this new variant all around the country (8). Periodic analysis of the results of a surveillance system in each country is very important for obtaining more knowledge about the nature, the impacts and the epidemiology of the intended disease (8).

## 2. Objectives

This report summarizes the results of a surveillance activity conducted on children aged 2 to 17 years in Khuzestan, south-western province of Iran, following the emergence of influenza A H1N1 virus between July 2009 and April 2010.

## 3. Patients and Methods

The study was approved by the Ethical Committee of Ahvaz Jundishapur University of Medical Sciences and informed consent was obtained from each patient included in the study. Patients who fulfilled the case definition criteria (5) and were from one of pediatric hospitals in the province of Khuzestan, Iran during July 2009–April 2010 were included in this study. A suspected case was defined as an individual presenting severe influenza-like-illness and respiratory complications with one or more of the following symptoms: nasal obstruction/rhinorrhea, sore throat, cough, fever (> 38°C), shortness of breath, and history of travel to affected areas within 7 days; or close contact with a confirmed or probable case of influenza A H1N1 within 7 days (8).

A questionnaire according to WHO pandemic influenza A H1N1 case summary form was completed for all suspected patients (9). Nasopharyngeal swab specimens were obtained by physicians. Specimens in a viral transport medium were transferred to the regional influenza reference laboratory in the virology department of Ahvaz Jundishapur University of Medical Sciences. All the clinical samples were kept at -70°C prior to the test (10). Viral RNA extraction was carried out for all the throat samples using high pure viral nucleic acid (Roche, Germany) according to the manufacturer's instruction. Initially influenza A was detected by using Real time Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) test according to the CDC protocol (5). Real-Time RT-PCR were carried out by the human influenza A H1N1 specific primers and probes on samples that were positive for influenza A virus, as recommended by CDC (11).

### 3.1. Statistical Analysis

Data are presented as means, standard deviations (SD) and percentages. The data were analyzed by SPSS, version 15. The following tests of significance such as, Kolmogrov-Smironov test was used to verify normal distribution of data. T-test was performed to compare age contraction amongst the two genders. Chi-square test was used to find out the homogeneity proportion among different age groups.

## 4. Results

The decision to admit patients to the hospital was taken according to the clinical condition of patients. All cases that fulfilled the case definition criteria (5) during July 2009–April 2010 were included in this study. During the study period, 232 throat samples were taken from children including 126 (54.31%) male and 106 (45.89%) female. The mean age of the male patients was 6.86 ± 4.21 (range 1-15 years) and the mean age of the female was 5.78 ± 3.87 (range < 1-14 years). On 5th of October, the first laboratory-confirmed case of influenza A H1N1 in Khuzestan was reported for an eleven-year-old boy. The results of the real-time reverse transcriptase-polymerase chain reaction showed that from the patients enrolled, 42 (18.1%) were confirmed positive for influenza A H1N1 virus. The frequency was higher during the period between weeks 43 and 46 (end of October to mid-November), shortly after the start of the educational year in Iran (September 23rd) (Figure 1). Isolation of confirmed cases was stopped on November 30th 2009, but sampling from suspected patients was continued till April 2010. Figure 2 shows age distribution of confirmed cases of influenza A H1N1 virus during the study period.
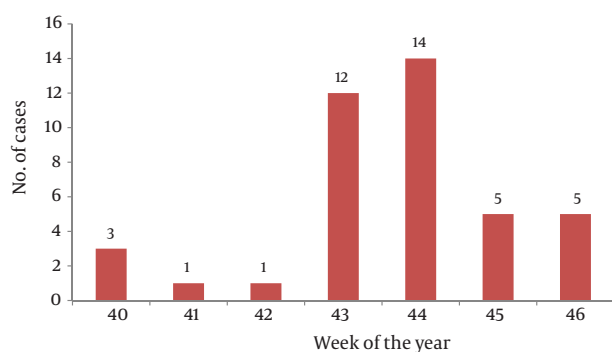
**Figure 1.** Distribution of Confirmed Cases of Influenza A H1N1 Virus Infection According to the Onset of Symptoms for Each Week

Median age was 9.34 ± 3 years (range 1.5–14); 19 were girls (38.1%) and 26 boys (51.9%). On average, patients were admitted to hospitals, 3 days (range 1-6) after symptom onset. Table 1 shows the clinical characteristics of patients. The most frequent symptoms were cough (34, 81%), fever (30, 71%), and myalgia (24, 57%) and five cases (12%) reported diarrhea. Information on clinical symptoms was available for 42 confirmed cases. None of the patients were vaccinated against pandemic influenza due to the unavailability of the vaccine in Iran at the time of the study and none of them died.

**Table 1.** Clinical Characteristics of the Patients With Confirmed Influenza A H1N1 Virus Infection (n = 42)

| Sign or Symptoms | Patients No. (%) |
|---|---|
| Cough | 34 (81) |
| Fever (T ≥ 38°C) | 30 (71) |
| Myalgia | 24 (57) |
| Headache | 23 (55) |
| Malaise | 20 (48) |
| Sore throat | 10 (24) |

**Figure 2.** Age Distribution of Confirmed Cases of Influenza A H1N1 Virus Infection During July 2009–April 2010
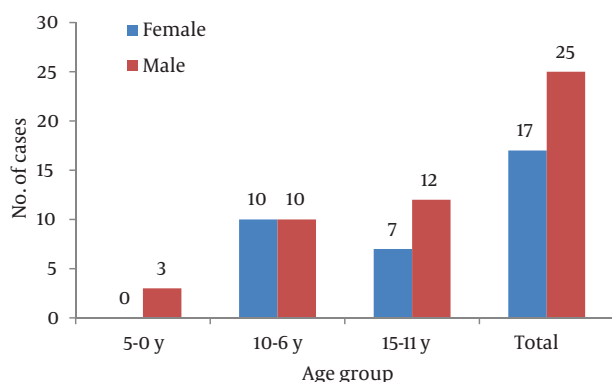


An asterisk (*) indicates a significant difference as indicated by a t-test.

## 5. Discussion

The Iranian Ministry of Health launched a system to monitor and report the presence of influenza A H1N1 virus throughout the country on May 10th, 2009 (12). Better understanding of the nature of influenza A H1N1 virus and its impacts on the health system, needs analysis of the results of surveillance in each province. In this report we summarize the results of a surveillance activity in southwestern province of Iran, Khuzestan, in response to the emergence of influenza A H1N1 virus during July 2009–April 2010.

The majority of cases were infected between weeks 43 and 46 (end-October to mid-November), shortly after the start of the educational year in Iran (September 23). Although sampling was continued until April 2010, no Influenza H1N1 case was detected after the end of November 2009. As you can see in Figure 2, the number of boys was greater than girls among the total number of confirmed cases. T-test indicated statistical significance between the two genders (P value < 0.05 with equality of variances). This maybe because, boys have greater contact with each other, and the risk of infection via contact among boys occurred sooner than girls. Evaluation of the first wave reveals male-female differences that vary between countries. Available data from Canada and Argentina showed that the incidence of influenza A H1N1 infection was higher in males than females for the 10–19 and 40–59 age groups, but the incidence was higher in females than males in France and Brazil for the 0–19 and 15–49 year olds. Unlike Belgium in Italy, and Peru no male-female differences were reported. Most reports of influenza A H1N1 infection do not analyze data for male-female differences (13).

The results of this study was similar to the results from other studies, in which the majority of influenza A H1N1 cases had been occurring in young people, with the median age estimated to be 12 to 17 years, like Canada, the USA, Chile, Japan, and the United Kingdom (14). Khuzestan was free of the pandemic virus during the whole first wave of the pandemics in the Northern Hemisphere and entered into the pandemic phase (phase V), with the confirmation of the 1st influenza A H1N1 case on the 5th of October, 2009. After just 2 weeks, the suspected cases peaked, confirming a shift into the pandemic peak period (phase VI), which coincided with the 2nd wave of pandemics in many countries of the Northern Hemisphere (Figure 1). When the suspected cases became lower than the upper tolerant limit, during January 2010, the pandemic had entered into the post-peak period (phase VII). On February 20th, 2010 Khuzestan entered the post-pandemic period (phase VIII) as no pandemic virus was detected for 3 months. Confirmation of influenza A H1N1 in young people who were mostly school children, decreased significantly after closing of schools and classes on November 4th. (See the difference between weeks 44 and 45 in Figure 1). Similar phenomenon was evident in some other

provinces of Iran (8).

Clinical signs and symptoms presented by patients infected with the influenza A H1N1 virus were similar to those described for seasonal influenza, although with more gastrointestinal disorders. In our series, up to 30% of cases presented vomits and 14% diarrheas, similar to other studies (2, 15-18).

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## Authors' Contribution

Study concept and design: Makvandi Manoochehr, Gooya Mohammad-Mehdi, Sorosh Mahmood, Nabavi Mahmood, Nikkho Abdol-Rassol, Nowrozibabaei Zahra, and Motlagh Mohammad-Esmaeil; Examinations and sample collection: Torabizadeh Mehd Doing the experiments: Neisi Niloofar, Nejati Ahmad, Najafifard Saied, Makvandi Kamyar, and Lotfi Soheila; Analysis and interpretation of data: Tarahomi Shahram, Amiri Homoyon, Ahmadi Kambiz, Dorostkar Hamidreza, and Askari Homaira;Drafting and preparing of the manuscript: Alvandi Amirhooshang and Aryan EhsanFinancial disclosure

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