

Original Article

Influenza A (H1N1) Pandemic in Iran: Report of First Confirmed Cases from June to November 2009

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Background: Since the declaration of a swine flu pandemic by the World Health Organization (WHO), the Islamic Republic of Iran has launched a surveillance system to test all suspected cases, both in community and hospital settings.

Patients and Methods: From June 1st to November 11th, 2009, there were 2662 (1307 females and 1355 males) RT-PCR confirmed cases of pandemic influenza A (H1N1) detected in Iran. Of these cases, 75% were 5 – 40 years-old. During this period, 58 patients (2.18%) died. Of the total number of cases, 33 were pregnant women with no reported mortalities amongst them. The prevalence of death had no significance correlation with sex and age ($P=0.720$ and 0.194 , respectively).

Results: Geographic distribution of the reported cases showed the highest rates in central and eastern provinces of Iran. There were two disease phases until November 2009, including an initial exogenous wave which blended into a second wave of indigenous disease, with a peak of cases after the start of the educational year. A review of the epidemiology of these initial phases of disease in Iran can help for better planning and more efficient action in future phases of the disease.

Conclusion: It is of utmost importance to strengthen the surveillance system for this disease and appropriately transfer the resultant knowledge to the medical professionals, stakeholders and the general population, accordingly.

Archives of Iranian Medicine, Volume 13, Number 2, 2010: 91 – 98.

Keywords: Epidemiology • influenza A (H1N1) • Iran • pandemic

Introduction

In April 2009, when health care staff in Mexico were trying to find the answer to why they had an unusual increase in the numbers of patients with respiratory diseases,

including pneumonia¹; no one could predict that a new type of influenza A (H1N1) would be reported in the majority of countries,² regions or communities with over 8000 deaths worldwide by the end of November 2009.³ Since the declaration of a swine flu pandemic by the World Health Organization (WHO) in April 2009,⁴ many countries have released the results of their surveillance systems.⁵⁻¹² Most of these reports are from America and Europe.¹³ In many countries this disease has had multiple waves until now and it is predicted that such waves would be repetitive in the coming months and even years.¹⁴ It is of extreme importance to analyze the results of the surveillance systems and periodically review the epidemiology of this pandemic in all countries in order to gain a better understanding of the nature

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Accepted for publication: 27 January 2010

of this disease and its impact. Through these reviews and reflections, better planning for future action would be possible. In May 2009, the Islamic Republic of Iran (IRI) launched a surveillance system to test all suspected cases, both in the community and hospital settings.¹⁵ In this study we aim to report the preliminary outcomes of this surveillance system until November 2009.

Patients and Methods

Case definition

A suspected case of H1N1 viral infection is defined as presenting with a high grade fever ($>38^{\circ}\text{C}$) or at least two acute respiratory symptoms including: nasal obstruction/rhinorhea, sore throat, cough, fever/feverishness and meets at least one of the following criteria:

- 1) Within the past seven days has returned from a country or region with an epidemic of H1N1,
- 2) In close contact (within two meters) with a confirmed case of H1N1 within the past seven days,
- 3) Has a moderate to severe respiratory illness requiring hospitalization, or unexplained or unusual clinical patterns associated with serious or fatal cases of H1N1.

A confirmed case of H1N1 is defined as a high grade fever ($>38^{\circ}\text{C}$) or at least two acute respiratory symptoms including: nasal obstruction/rhinorhea, sore throat, cough, fever/feverishness and H1N1 viral infection that has been confirmed by reverse transcriptase PCR (RT-PCR).

H1N1 influenza-related death is defined as any person with a confirmed H1N1 infection in an ante mortem or post mortem specimen, and who died from a clinically compatible illness or complications attributable to that infection, with no complete recovery period between the illness and death and no alternative cause of death.

Surveillance

Since September 2005, a surveillance system for the detection of avian flu has been launched in our country in order to test all patients admitted to public hospitals with a diagnosis of severe community acquired pneumonia and/or acute respiratory distress syndrome for avian flu. Shortly after the official declaration of the first human cases of H1N1 by the WHO, the Ministry of Health and Medical Education (MOHME) of IRI added a new H1N1 nationwide case definition to

the present surveillance system. MOHME supplied all Provincial Universities of Medical Sciences (PUMS) with case definitions and surveillance questionnaires to be disseminated to all healthcare institutions in their provinces. These forms contained questions regarding demographic data and clinical information of suspected cases of H1N1. Each PUMS designated special referral hospitals and clinics for all public health facilities, including coverage of referrals from more than 17,000 health houses nationwide. These special centers were equipped with nasopharyngeal swabs and a sample referral system to regional and national influenza laboratories. The designated centers were asked to take samples from patients who fulfilled the case definition criteria and send them for confirmation to the designated reference laboratories. Similar strategies were used for those patients with severe pneumonia and respiratory distress who were hospitalized. Each PUMS sent the information of confirmed cases to the Influenza Surveillance Center of IRI's MOHME.

Patients and samples

For all patients who met the aforementioned criteria as suspected cases, nasal and throat swabs were taken and samples examined by RT-PCR protocol distributed by the United States Centers for Disease Control and Prevention (US CDC) for the detection and characterization of pandemic H1N1 virus, as recommended by WHO.¹⁶ Information about confirmed cases was recorded on national forms and each form was sent to the PUMS' Centers for Pandemic Influenza. Since declaration of the pandemic by WHO on June 2009, MOHME has formed a national committee to evaluate the H1N1 pandemic in IRI. The committee approved the following as its priorities: educating people via national broadcasting, providing adequate stockings of oseltamivir and other necessary drugs including other antivirals and antibiotics, designing a national protocol for case definition, as well as diagnosis and evaluation of the provincial preparedness plan. Each PUMS was asked to educate all health care providers in its territory, whether working in private or public hospitals, about the disease. A mandatory course for all physicians working in the country was launched on June 2009 in order to inform them of the new pandemic flu virus (H1N1). Close attention was paid to the country points of entry, including Umrah pilgrims, in airport terminals. All travelers from abroad were requested to declare

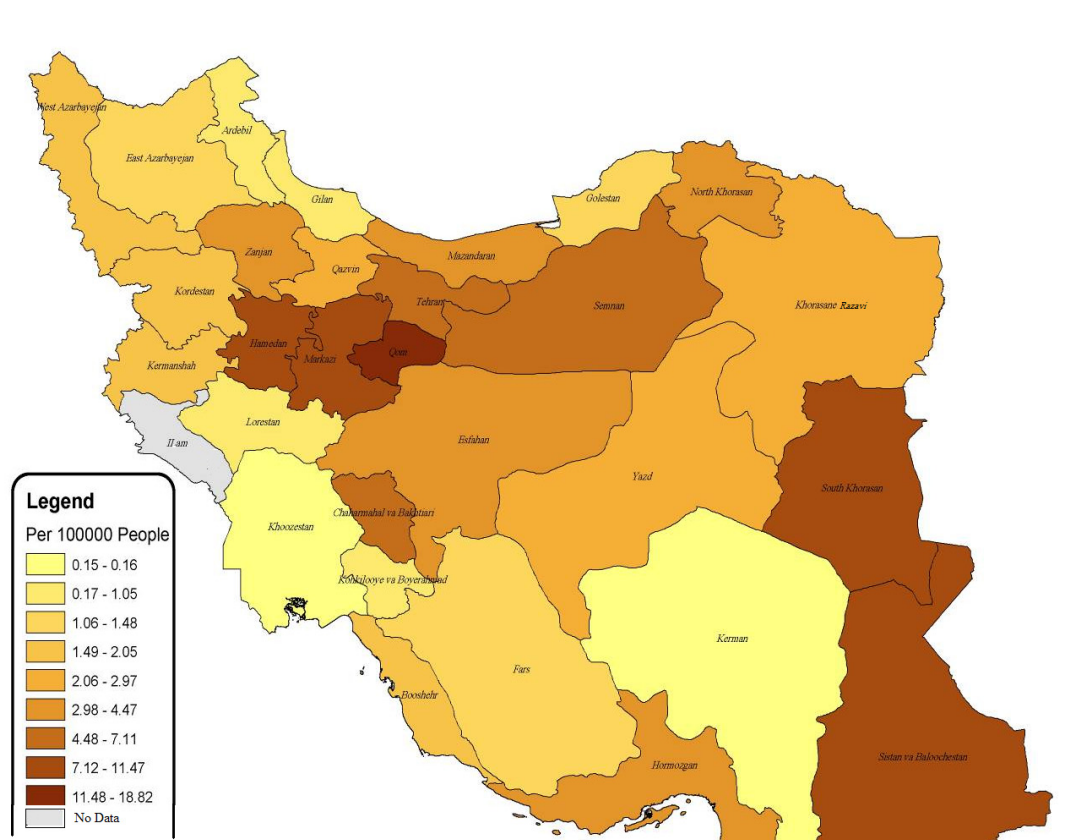


Figure 1. Geographic distribution of reported confirmed cases of H1N1 in Islamic Republic of Iran

their health status and those who had complaints of influenza-like illness were further examined by physicians and suspected cases were referred to the designated referral centers mentioned above. Furthermore, millions of pamphlets and posters providing information on the flu pandemic were distributed through the country and airports to increase community awareness. Finally, based on the national protocol, confirmed or suspected cases under certain circumstances after sampling (after RT-PCR) received oseltamivir (75 mg twice daily for five days).

Results

Since June 1 to November 11, 2009, 2662 (1307 females and 1355 males) individuals, who presented with flu-like illnesses, were confirmed swine flu patients in Iran. The mean age was 22.6 years old (SD=16.0, range from 5 days old to 96 years old). Of these, 756 (29.3%) patients were in the age group 5 – 15 years old and 1197 (46.2%) in the age group of 15 – 40 years old (Figure 1). As of November 11th, there were 58 patients (2.18%)

who died and the mean age of these cases was 26.5±20.6 years old. Of the reported deaths, 13 cases were students (either from universities or primary and secondary schools). The death prevalence had no significance correlation with sex and age ($P=0.321$ and 0.052 , respectively; Table 1). Geographic distribution of the reported cases showed the highest rates to be in the central and eastern provinces of Iran (Figure 1). There were 33 H1N1 cases that were pregnant, with no reported mortalities among this group. The mean time

Table 1. Mortality percentage in each age group of confirmed H1N1 cases in Islamic Republic of Iran

AGE	Confirmed cases of H1N1	
	Total	Death No. (%)*
Under one year	70	5 (7.1)
1 – 5 years	135	3 (2.20)
5 – 15 years	717	12 (1.7)
15 – 40 years	1266	27 (2.1)
40 – 65 years	330	8 (2.4)
More than 65 years	59	3 (5.1)

*P value of 0.052.

between onset of symptoms and nasal/throat swab sampling was 2.7 days (SD=2.3, range 0 to 9 days) while the mean time between sampling and preparation of the results was 1.9 days (SD=1.7, range 0 to 12 days).

The prevalence was highest in October 2009 (Figure 2). Shortly after the start of the educational year in Iran (September 23, 2009), the total number of cases increased slightly but a peak of new cases occurred two weeks later. From the last week of October we witnessed a decrease in the number of patients and this trend continued until the first half of November. Detailed data of 830 patients was available at the time of preparing this report. Among them, 511 had a history of fever, 406 patients had a history of body pain, while cough was the primary complaint in 465 patients. Out of these 830 patients, 12 patients had received the seasonal flu vaccine and 238 (28.7%) of them had a history of travel abroad with different starting points as mentioned in Figure 3.

Discussion

This is the first report of confirmed cases of pandemic H1N1 2009 influenza from Iran. From

June 2009 to November 11th, 2009, 2662 confirmed cases of this disease were documented in Iran. Apparently, during this period, the disease had at least two waves in this country. In the early stages of the disease in Iran, the role of foreign travel was prominent. This pattern was similar to the findings of other studies.^{10-12,17,18} For instance, in China, through the first wave of the disease, 32.9% of the patients were imported cases.¹⁹ The first case in Iran was an Iranian student living in the U.S.A. who came to Iran for summer vacation and developed symptoms less than a week after his arrival.²⁰

Approximately 70% of the first 500 cases had either a history of travel abroad during the previous two weeks before their influenza like illness symptoms or had contact with someone who returned from abroad. The most common starting point was the Kingdom of Saudi Arabia (KSA) for Umrah. Based on the estimation of Iranian officials in the year 1387, concordant with 2008 – 2009 AC, each week, approximately 120,000 Iranian people left Iran for short term travel.²¹ An estimated 25 – 30000 of the travelers' destination was KSA for Umrah.²² However, the number of patients with swine flu was unexpectedly much higher among

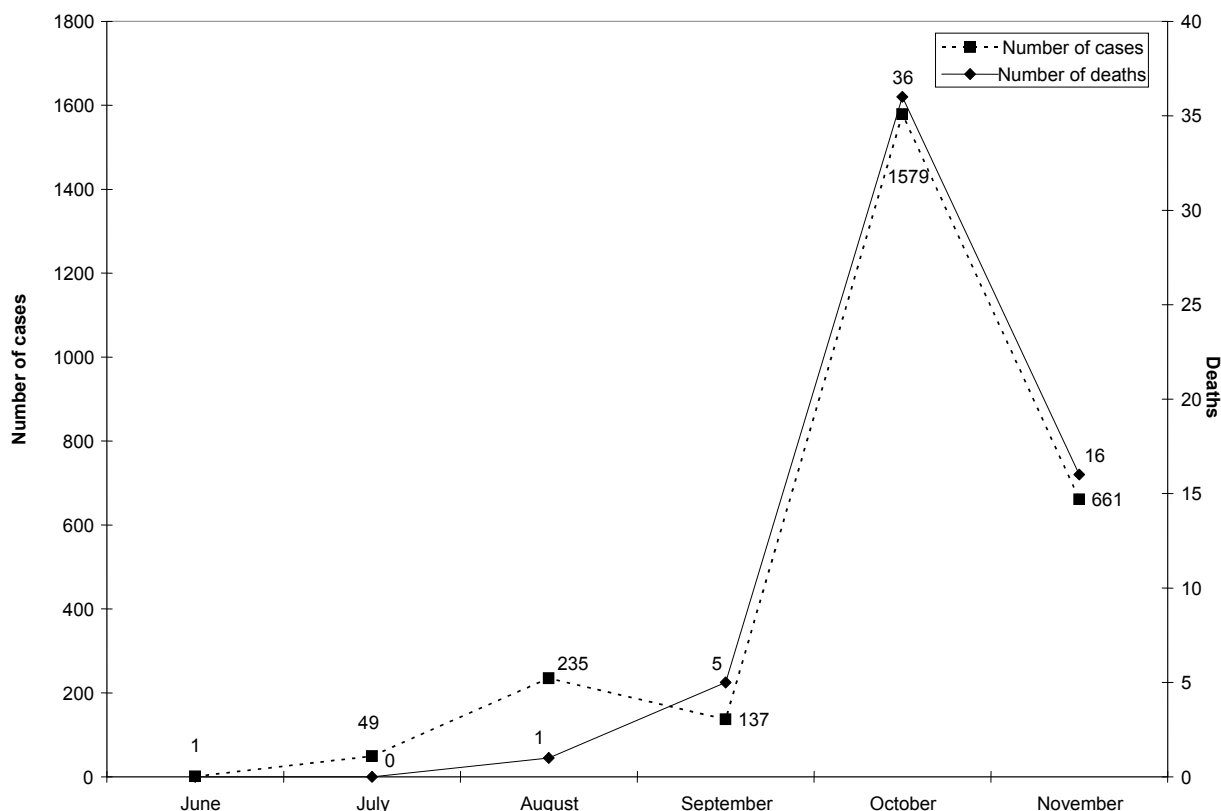


Figure 2. Frequency of confirmed cases of H1N1 from June 1 to November 15, 2009 in the Islamic Republic of Iran

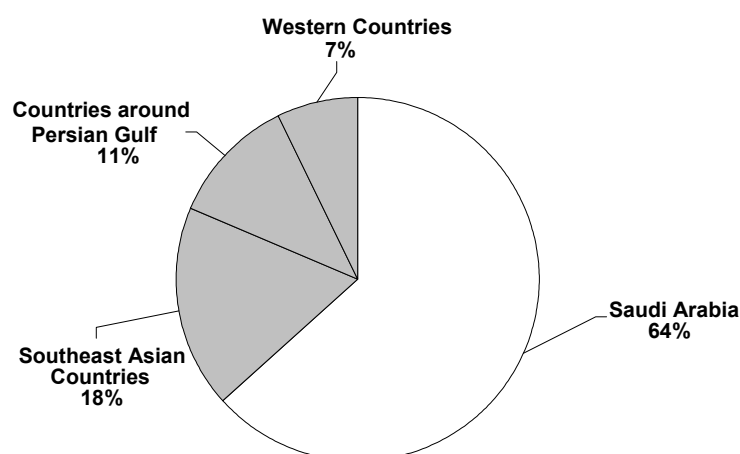


Figure 3. Distribution of starting points among those who had a history of travel abroad

Iranian visitors to KSA compared to other countries. This higher reported rate of disease from travelers to KSA and their close contacts might be related to worse health conditions there or more awareness of the surveillance system among these travelers. Another possibility was the closer contact of these pilgrims after their return with their relatives. As this travel is considered a religious travel, close contacts such as hugging and kissing are more likely to occur upon their arrival as compared to other trips. In reality, after the pilgrimage to Umrah was stopped, which was implemented in late August, the number of cases dropped dramatically.²³

The effect of foreign travel was reduced with an increased number of indigenous cases, especially after the start of the education year in late September 2009. In the second wave of the disease, the numbers of patients requiring hospitalization and the total numbers of deaths increased dramatically. We have seen the same scenario in different parts of the world.²⁴⁻³⁰

As mentioned before, in the second wave most of the confirmed cases were students either in schools or universities. Moreover, of patients who died, there were 13 students. Since this second wave of disease occurred after the start of the education year in Iran, one of the major transmission modes could be transmission in the schools and universities. By following some successful experiences of school or class closures under certain circumstances to mitigate the spread

of this infection³¹⁻³⁶, this strategy was adopted by the National Committee for the Control of Flu in Iran. After a surge of infection during the first few weeks of this education year, once this strategy was implemented, a dramatic decrease in new cases occurred in some of the provinces. For example in Sistan Baloochestan and Tehran Provinces, after implementation of the school class closure program, the number of new cases diminished up to 50%.

As we can only detect a small percentage of those who are symptomatic in any surveillance program, the true extent of disease during the first weeks of the education year might have been much higher.

Only 33 of the first 830 cases were pregnant, of which none died during this period. This is in contrast to several other reports that indicated 10% of hospitalizations and deaths were from pregnant women.³⁷⁻³⁹ In the early 1990s a national surveillance system was implemented in the country for registration of adverse events during pregnancy and the post-partum period. Through national programs for achieving millennium development goals (MDGs) this system has recently strengthened.^{40,41} Although there is the possibility of under-reporting in maternal mortality, it seems the extent of such under-reported data should not be very high. This lower rate of disease in the pregnant population might be related to the younger age of pregnancy in Iran compared to western countries.⁴²⁻⁴³ The younger

age of pregnant women has probably resulted in lower rates of co-morbid conditions and consequently a healthier base line status. This should be confirmed in greater detail with long-term comparative studies.

Although the available data were not adequate to find special risk factors for the disease itself, or its severity, more than 70% of our cases were younger than 40 years as reported in other countries.⁴⁴⁻⁴⁶ For those who died, the mean age was 26.5 ± 20.6 years old and approximately 80% were less than 40 years of age. Although no statistically significance relation could be found between the age of patients and risk of death, but there was a trend toward a lower mortality rate among those aged less than one year or greater than 65 years. The same trend has been seen in other countries.⁴⁷⁻⁴⁸ This means we are witnessing a pandemic affecting the most active and productive part of the communities and this should be considered in any preventive plan.

As of December 23, 2009, the global death toll of H1N1 virus has continued to grow to over 11500 cases.³⁰ The death rate in the Eastern Mediterranean Region (EMR) of WHO has risen to 663 by December 19, 2009.⁴⁹ Under-reporting in the number of infected cases and also in the number of deaths due to swine flu is a main point of concern worldwide, however, to some extent it is a more challenging issue in EMR countries. The

sensitivity of surveillance systems in these countries and also their health system backbone are quite different. In addition, their policies in reporting health information vary. It is worth noting that the data of some countries had not been updated for weeks. High numbers of confirmed cases in some countries could be solely because of more active case findings, while very low numbers of mortality may imply fragile reporting systems.

To minimize the impact of under-reporting, we can estimate the death ratio which is the number of deaths per one million population. Assuming comparable attack and virulence rates, we do expect a similar death ratio in different countries. Since the number of deaths is recorded more accurately when compared to the number of confirmed cases; the death ratio is a more stable indicator.

Based on the above explanation, we computed the death ratio in Iran and in some of its neighboring countries using data from WHO EMRO and the official website of the Ministry of Health in Turkey (Figure 4).^{49,50} The death ratio in Iran was approximately 1.99 per million people, which is close to the death ratio in Iraq (1.35) and the United Arab Emirates (1.33).

We had some drawbacks in this report which include: the lack of reports from some regions in Iran such as Ilam Province (Figure 1), and limitations in providing demographic and clinical

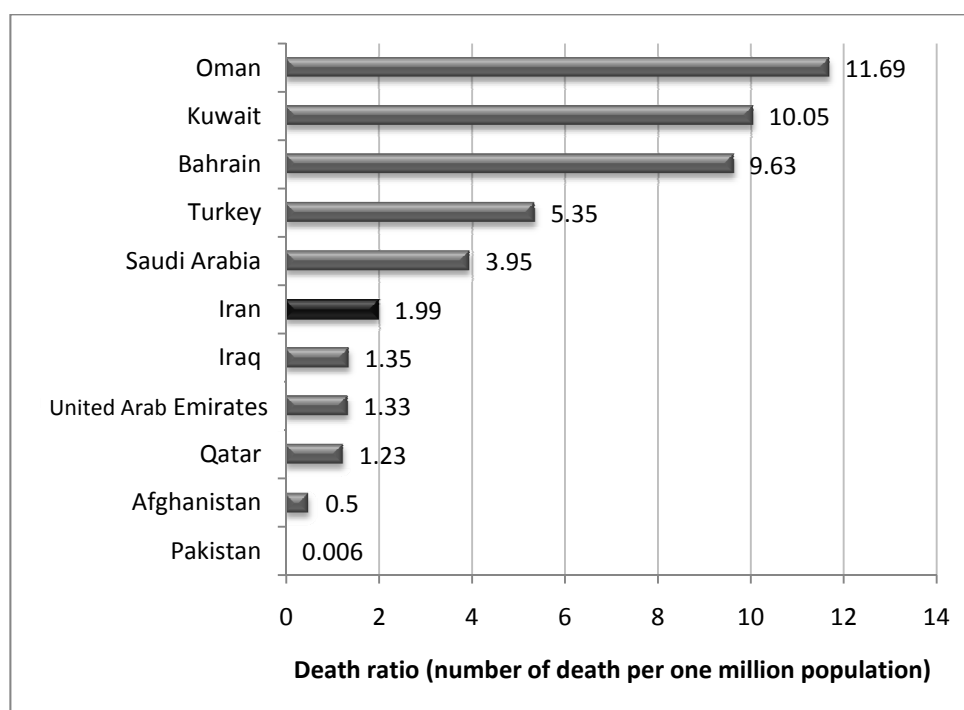


Figure 4. Death ratios in the Islamic Republic of Iran and some neighboring countries

information for each patient. We hope to waive these limitations in future reports by improvement of our surveillance system.

As we are still in the first few months of this pandemic the true extent of this new infection is not yet clear. The total number of cases in this report is underestimated as many mild cases are not tested and remain undiagnosed. However, the number of deaths might be more accurate as the system is more alert for detecting severe cases and deaths. For more precise estimation of the impact of H1N1 pandemic in Iran, application of disease modeling can be helpful.⁵¹

It is of utmost importance to strengthen the surveillance system for this disease and transfer the generated knowledge appropriately to medical professionals, stakeholders and the general population, accordingly.

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