Influenza A(H1N1) pandemic in Iran: Report of first confirmed cases from June to November 2009

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Abstract:

Since declaration of swine flu pandemic by world health organization (WHO), Islamic republic of Iran (IRI) has launched a surveillance system to test all suspected cases both in community and hospital settings. From Jun 1 to November 11, 2009, 2662 (1307 females and 1355 males) RT- PCR confirmed cases of pandemic influenza A(H1N1) were detected in Iran. Seventy five percent of cases were 5-40 year-old. Fifty eight patients (2.18%) died. Of the total, 33 cases were pregnant women with no mortality report among them. The prevalence of death had no significance correlation with sex and age (P=0.720 and 0.194 respectively). Geographic distribution of reported cases showed highest rates in central and eastern provinces of IRI. Disease had two phases till November 2009, including an initial exogenous wave blending to a second wave of indigenous disease with a peak of cases after starting of education year. Review of the epidemiology of these initial phases of disease in IRI can help for better planning and more efficient action in further phases of disease. It is of utmost importance to strengthen the surveillance system for this disease and transfer the generated knowledge appropriately to the professionals, stakeholders and general population accordingly.

Key Words: Influenza A(H1N1), Iran, Pandemic, epidemiology
Introduction

When health care staff of Mexico in April 2009 were trying to find the answer of why they had unusual increased number of patients with respiratory diseases including pneumonia (1), nobody could guess that a new type of influenza A (H1N1) would be reported in almost all countries (2), regions or communities with over than 8000 deaths worldwide just by the end of November 2009 (3). Since declaration of swine flu pandemic by World Health Organization (WHO) in April 2009 (4), many countries have released result of their surveillance systems (5-12). Most of these reports come from America and Europe (13). In many countries the disease had multiple waves till now and it is predicted such waves would be repetitive in next month and even years (14) It is of extreme importance to analyze the result of surveillance system and review the epidemiology of this pandemic periodically in every country for better understanding of the nature of this disease and its impacts. Through these reviews and reflections better planning for future action would be possible. Islamic republic of Iran (IRI) has launched a surveillance system since May 2009 to test all suspected cases both in community and hospital settings (15). In this report we presented the preliminary result of this system as late as November 2009.

Methods

a. Case Definition

A suspected case of influenza A (H1N1) virus infection was defined as one who has high grade fever (>38°C) or has at least two acute respiratory symptoms including; nasal obstruction/rhinorrhea, sore throat, cough, fever/feverishness) and met at least one of the following criteria:

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

A confirmed case of influenza A (H1N1) was defined as one who has high grade fever (>38°C) or has at least two acute respiratory symptoms including; nasal obstruction/ rhinorrhea, sore throat, cough, fever/
feverishness) and influenza A (H1N1) v virus infection that has been confirmed by Reverse Transcriptase PCR (RT-PCR).

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

b. Surveillance

Since September 2005 a surveillance system for detection of avian flu was launched in the country testing all hospital admissions with diagnosis of severe community acquired pneumonia and/or acute respiratory distress syndrome for avian flu in all public hospitals. Shortly after the official declaration of the first human cases of new influenza A (H1N1) by the WHO, the Ministry of Health and Medical Education (MOHME) of Islamic republic of Iran added a new H1N1 nationwide case definition to the present surveillance system. Every Provincial University of Medical Sciences (PUMS) was supplied by the MOHME with case definitions and surveillance questionnaires to be disseminated to all healthcare institutions in their province. These forms contained questions regarding demographic data and clinical information of suspected cases of influenza A (H1N1). Each PUMS assigned especial 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 prepared reference laboratories. Similar strategies were used for those patients with severe pneumonia and respiratory distress who were hospitalized. Every PUMS sent the information of confirmed cases to the influenza surveillance Center of MOHME of IRI.

c. Patients and samples

From every patient who met afore mentioned criteria as a suspected case, nasal and throat swabs were taken and samples were examined by using the Reverse Transcriptase PCR (RT-PCR) protocol distributed by the United States Centers for Disease Control and Prevention (US CDC) for the detection and characterization of pandemic influenza A (H1N1)v virus as recommended by WHO (16). The information of confirmed cases was recorded in a national forms and each form was sent to PUMS center of pandemic influenza. Since declaration of the pandemic by WHO on June 2009, the MOH of IRI has formed national committee for evaluation of situation of the influenza A (H1N1) pandemic in country. The committee approved its priorities on people education via national
broadcasting, providing Pill stocking of oseltamivir and other necessary drugs including other antiviral and antibiotics, designing a national protocol for case definition, 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 to aware all of them about the new pandemic flu virus (H1N1). Closed attention was paid to the country points of entry including Umrah pilgrims’ in airport terminals. All travelers from abroad were requested to declare their health status and those who had complaint of influenza like illness was further examined by physicians and suspected cases were referred to designed referral centers mentioned above. Furthermore millions of pamphlets and posters providing information on the flu pandemic were distributed through the country and airports to community awareness. Finally based on national protocol confirmed or suspected case under certain circumstances after sampling received oseltamivir (75mg twice daily for 5 days).

Results

Since June 1 to November 11, 2009, 2662 (1307 females and 1355 males) individuals, who presented with flu like illness, were confirmed as swine flu patients in Iran. Mean age was 22.6 year-old (SD=16.0, range from 5 day-old to 96 year-old). Seven hundred and fifty six (29.3%) of patients were in age group 5-15 year-old and 1197 (46.2%) in age group of 15-40 year-old (figure 1). Fifty eight patients (2.18%) have died up to November 11 and Mean age of these dead cases was 26.5± 20.6 years old. Thirteen of reported death cases were students (either from universities or schools). The prevalence of death had no significance correlation with sex and age (P=0.321and 0.052 respectively) (Table 1). Geographic distribution of reported cases showed highest rates in central and eastern provinces of Iran (figure 1). Thirty three of the influenza A (H1N1) cases were pregnant women with no reported mortality among this group. Mean time between start 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 day (SD=1.7, range 0 to 12 days).

The prevalence was highest in October 2009 (figure 2). Shortly after start of 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 number of patients and this trend have continued up to first half of November. Detailed data of 830 patients were available by the time of preparing this report. Among them 511 gave history of fever and 406 patients had history of body pain
while cough was complaint of 465 patients. Out of these 830 patients 12 patients received seasonal flu vaccine and 238 (28.7%) of them had history travel to abroad with different starting points mentioned in figure 3.

<table>
<thead>
<tr>
<th>AGE</th>
<th>Confirmed cases of H1N1</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
</tr>
<tr>
<td>Under one year</td>
<td>70</td>
</tr>
<tr>
<td>1-5 years</td>
<td>135</td>
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<tr>
<td>5-15 years</td>
<td>717</td>
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<tr>
<td>15-40 years</td>
<td>1266</td>
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<tr>
<td>40-65 years</td>
<td>330</td>
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<tr>
<td>More than 65 years</td>
<td>59</td>
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</tbody>
</table>

* P value was 0.052.

Table 1: Mortality percentage of each age group of confirmed cases of swine flu in Islamic Republic of Iran.
Figure 1: Geographic distribution of reported confirmed cases of H1N1 influenza in Iran
Figure 2: Frequency of confirmed cases of swine flu from Jun 1 to November 15, 2009 in Islamic Republic of Iran.
Figure 3: Distribution of starting points among those who had travel history to abroad.
Discussion:

This is the first report of confirmed cases of pandemic H1N1 2009 influenza from IRI. From June 2009 to 11th November 2009, 2662 confirmed cases of this disease were documented in IRI. Apparently the disease had at least two waves in this country during this period. In the early stage of the disease in Iran, 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 disease, 32.9% of patients were imported cases (18). The first case in Iran was an Iranian student living in United States of America (USA) who came for summer vacation to Iran and developed symptoms in less than a week after his arrival (20).

Approximately 70% of first 500 cases had either history of travel aboard in past two weeks before their ILI or had a contact with someone who returned from such a travel. The most common starting point was Kingdom of Saudi Arabia (KSA) for Umrah. Based on the estimation of Iranian officials in the year 1387, concordant with 2008-2009 AC, every week near 120,000 Iranian people leave Iran for a short term travel (21). For up to 25 -30000 of them the destination was KSA to do Umrah(22). But the number of patients with swine flu was unexpectedly much higher among Iranian visitors to KSA compared to other countries. This higher reporting rate of disease from travelers to KSA and their close contacts might be related to worse health condition there or more awareness of the surveillance system to these travelers. Another possibility is closer contact of these pilgrims after their return with their relatives. As this travel is considered a holey travel, close contacts such as hugging and kissing are more likely to occur upon their arrival compared to other trips. In reality after stopping sending pilgrims to Umrah which was implemented on late August the number of cases dropped dramatically. (23)

The effect of foreign travel was reduced with increased number of indigenous cases especially after start of the education year in late September 2009. In the second wave of disease, the number of patients requiring hospitalization and the total number of death raised dramatically. We see the same scenario in different parts of the world (24-30).

As mentioned before, in the second wave, most of confirmed cases were students either in schools or universities. Moreover among died patients we had 13 students. Since this second wave of disease occurred after start of education year in Iran, one of the major transmission modes could be transmission in the schools and universities. Building on some successful experiences of school or class closure under certain circumstances in mitigating spread of this infection (31-36) , this strategy was adopted by the national committee for the control of flu in IRI. After a surge of infection in first few weeks of this education year, once this strategy was implemented, a dramatic decrease in new cases occurred in some provinces. For example in Sistan Balochestan and Tehran provinces, after implementation of 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 in the first weeks of education year might have been much higher and the apparent decrease might be only related to previous infection of most that were susceptible.

Only 33 of the first 830 cases were pregnant ladies. None of them died in this period. This is in contrast to several other reports indicating 10% of hospitalization and deaths were among pregnant women (37-39). In the early 1990s a national surveillance system has been implemented in the country for registration of adverse events during pregnancy and post partum period. Through national programs for achieving millennium development goals (MDGs) this system has recently strengthened (40, 41). Although still there is possibility of under reporting of maternal mortality, it seems the extent of such missing data should not be so high. This lower rate of disease in 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 probably resulted in lower rates of co-morbid conditions and consequently a healthier base line status of them. This should be confirmed in more detailed in comparative studies in long term.

Although the available data were not adequate to find special risk factors for 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 have died the mean age was 26.5 +/- 20.6 years old and about 80% of them were aged less than 40 years. Although no statistically significance relation could be found between the age of patients and risk of death but there was a trend toward higher mortality rate among those aged less than one year or more than 65 years. The same trend has been indicated by 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 23 December 2009 the global death toll of H1N1 virus continued to grow to more than 11,500 cases (30). The death rate in Eastern Mediterranean Region (EMR) of WHO rose to 663 as 19 December 2009 (49). Underreporting in the number of infected cases and also in the number of death due to Swine flu is a main point of concern around the world, however to some extend 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 their health information vary. It is worth noting that the data of some countries were not updated for weeks. High number of confirmed cases in some countries could be just because of more active case findings, while very low number of mortality may implies fragile reporting systems.

To minimize the impact of underreporting, we can estimate death ratio which is the number of death in one million populations. Assuming comparable attack and virulence rates, we do expect similar death ratio in different countries. Since, the number of deaths is recorded more accurately comparing to the number of confirmed cases; death ratio is a more stable indicator.
Based on the above explanation, we computed the death ratio in Iran and in some of its neighborhood countries using data from WHO EMRO and official website of Ministry of Health of Turkey (figure 4) (49, 50). Death ratio in Iran was around 1.99 per million populations which is close to the death ratio in, Iraq (1.35) and United Arab Emirate (1.33).

![Death ratio in Iran and some neighbor countries](image)

**Figure 4: Death ratio in Iran and some neighbor countries**

We had some drawbacks in this report including; lack of report from some regions in Iran such as Ilam province (Figure 1) and limitation in providing demographic and clinical information for every patient. We hope to waive these limitations in following reports by evolution 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 an under estimate as many mild cases are not tested and not diagnosed. But the number of deaths might be more accurate as the system is more alert for detecting severe cases and deaths.

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