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ORIGINAL ARTICLE

Influenza A (H1N1) Virus Pandemic in Fars Province: A Report from Southern Iran, July-December 2009

M Moghadami[1,2], P Afsar Kazeroni[1], B Honarvar[1], M Ebrahimi[1], H Bakhtiari[1], MA Akbarpour[1], HR Tabatabaee[3], AR Mirahmadizadeh[3], A Rezaianzadeh[3], J Hasanzadeh[3], N Zamiri[2], B Sabayan[2], A Moattari[4], A Emami[4], KB Lankarani[2]*

[1]Deputy of Health, [2]Health Policy Research Center, [3]Department of Epidemiology, [4]Department of Virology, Shiraz University of Medical Sciences, Shiraz, Iran

Abstract

Background: Influenza type A (H1N1) virus is considered as a major concern for health care system all over the world and imposes a considerable burden on the community. The aim of this study was to evaluate the pattern of the disease in order to help health administrators in making decision for preventive measures.

Methods: 297 definite cases of influenza A (H1N1) diagnosed from 15 July to 3 December 2009 in Fars province, south of Iran, were included in this study. Diagnosis was confirmed performing Real time-PCR. The patients' information including age, gender, occupation, nationality, education, residency area and history of overseas or domestic travel, history of contact with other influenza patients, and symptoms were collected and analyzed.

Results: The mean age at the time of diagnosis was 24.4±15.8 years. 76 (25.6%) patients were admitted in the hospitals, of whom, 11 cases died due to related influenza complications with Case Fatality Ratio (CFR) of 4.4%. The most common reported symptoms were fever, cough and sore throat. There were two waves in the disease incidence, one about 1 month after emergence of the disease and another around 1 month after school openings. The first peak was observed mainly among adults with a history of foreign travel while the second peak was mainly observed among school students.

Conclusion: The magnitude of the epidemic was much higher when the disease was transmitted between students at the beginning of the school year. Considering the high incidence of H1N1 flu among the students (41%), vaccination programs and preventive measures should target this age group.

Keywords: H1N1 influenza; Incidence; Mortality; Comorbidity; Iran

Introduction

Ever since March 2009, influenza type A (H1N1) virus has emerged as a major health issue for individuals and has been a great burden on the health care system worldwide.[1,2] The disease was first diagnosed in Mexico in May 2009 and shortly after that in the United States of America (USA) in April 2009. Since then, the pandemic has quickly spread throughout the world.[3] On 24th of April 2009, the World Health Organization (WHO) issued a global warning regarding the H1N1 influenza virus and announced the disease pandemic.[3] By 17 January 2010, more than 209 countries and overseas territories have reported laboratory confirmed cases of pandemic influenza H1N1 2009, including at least 14142 deaths.[4]

Several countries have released primary reports regarding the status of the pandemic in their societies. So far, most of them have been reported from America and Europe.[5-8]

Due to similarities of the symptoms to other respiratory illnesses, diagnosis is one of the major issues in management of this pandemic. Based on the esti-

***Correspondence:** Kamran Bagheri Lankarani, MD, Professor of Gastroenterohepatology Research Center, Health Policy Research Center, Shiraz University of Medical Sciences, Shiraz, Iran. Tel: +98-711-6474263, Fax: +98-711-6474263, e-mail: lankaran@sums.ac.ir
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mations by the Centers for Disease Control and Prevention (CDC), only 5 to 10 percent of the cases are detectable depending on surveillance strategies.[9] Therefore, case definition and surveillance methods are of great importance in the study of H1N1 flu epidemiology.

In order to provide a better management and preventive plan for this pandemic, a thorough and concise evaluation of the pattern of spread and age and sex distribution of the disease seems inevitable. On the other hand, lack of advanced diagnostic facilities is one of the most important obstacles regarding diagnosis and better study of the disease especially in developing countries.[10] In this study, we aimed to investigate the epidemiologic curve and pattern of disease spread with regard to the demographic factors in southern Iran which is the preliminary report of a large ongoing study on H1N1 influenza.

Materials and Methods

The statistics of H1N1 pandemic in Fars Province, Southern Iran, were gathered benefitting from the already active national surveillance system that has been implemented by Islamic Republic of Iran's Ministry of Health in collaboration with each Provincial University of Medical Sciences throughout the country.[11]Based on multiple expert panels and workshops at the beginning of the pandemic in Iran and the ongoing experience with surveillance of Avian flu (started at September 2005), a surveillance system for detection of H1N1 flu was launched in the country shortly after the announcement of first human cases of new influenza A (H1N1) by World Health Organization (WHO). Hence, the case definition of the new H1N1 influenza was added to the present surveillance system by The Ministry of Health and Medical Education (MOHME) of Islamic Republic of Iran.

A suspected case of H1N1 influenza virus infection was defined as: Presence of high grade fever (>38°C) or at least two of the following acute respiratory symptoms including nasal obstruction/rhinorrhea, sore throat, cough, fever/ feverishness and meeting at least one of the following criteria: 1) has returned from a country or region with an epidemic of H1N1 influenza within the last seven days, 2) has been in close contact (within two meters) with a confirmed case of H1N1 influenza within the past seven days and 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 was defined as a patient who had the mentioned criteria (regarding the symptoms, fever or two of the acute respiratory illness symptoms) and for whom H1N1 influenza virus infection was confirmed by Reverse Transcriptase-Polymerase Chain Reaction (RT- PCR) method. H1N1 influenza-related death was defined as any case of fatality for whom H1N1 influenza infection was confirmed by RT-PCR and had died due to complications attributed to H1N1 influenza, with no period of complete recovery between the illness and patient's death and no alternative cause of death.

Shiraz University of Medical Sciences as other similar authorities in the country was designated as the representative of MOHME in Fars Province concerning the implementation and supervision on the surveillance system. All health care providers in Fars Province (public or private) from health houses in rural areas to hospitals and clinics in urban areas of Fars province were oriented about the process and the necessity of reporting the disease based on national case definitions provided and distributed by MOHME of Islamic Republic of Iran. Special centers in Shiraz, Province capital, were assigned as referral centers for Fars Province. These special centers were equipped with nasopharyngeal swabs and a sample referral system to regional and national influenza laboratories. Patients who fulfilled the case definition criteria were referred to these centers for sampling and confirmation of the diagnosis. Similar strategies were used for those patients with severe pneumonia and respiratory distress who were hospitalized. All travelers from abroad were requested to be examined for their health status and further evaluation was performed for that influenza-like illness symptom by physicians and suspected cases were referred to referral centers.

The first confirmed case of H1N1 influenza in Fars province was diagnosed by 15 July 2009 and until 15 December 2009, 297 patients among the suspected cases were diagnosed as H1N1 influenza after nasal and throat swabs were taken and the samples were tested using RT- PCR. The protocol for PCR was based on the guidelines distributed by United States Center for Disease Control and Prevention (US CDC) for detection and characterization of pandemic influenza A (H1N1) virus recommended.[11]

Every patient for whom the diagnosis of H1N1 influenza was confirmed underwent a thorough interview and data regarding demographic characteristics

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and their symptoms were gathered. The data were analyzed using SPSS software program (version 15, Chicago, IL, USA). T test was used for comparing two means and Chi Square for qualitative data. A *p* value<0.05 was considered as statistically significant.

Results

From June to mid December 2009, 297 individuals, who presented with flu-like illness, were diagnosed to have developed Swine-origin H1N1 flu using RT-PCR method.

149 (50.2%) were female with a mean age of 24.4±15.8 years ranging from 1 to 84 years. The complete demographic characteristics of the subjects are shown in Table 1.

The patients were further divided into several sub-groups according to their age range. The majority of them were in the age group of 15-40 years which included 150 cases (54.5%). Seventy five cases (27.3%) were in the 5-15 year age group. The age distribution of H1N1 flu in the population is shown in Figure 1.

Regarding the occupational status, 103 (41.0%) cases were elementary or high school students, 17 (6.8%) were college students and 58 (23.1%) were housewives. Figure 2 demonstrates the trend of changes in pandemic flu incidence in students compared to other occupations.

Thirty two patients had a history of traveling from abroad from March 2009. 71 (23.9%) cases had a history of prior contact to subjects with flu-like illness symptoms. Seventy six (25.6%) patients were admitted in hospitals among whom, 11 cases died due to related influenza complications with Case Fatality Ratio (CFR) of 4.4%. Among those who died, the

Table 1: Summary of demographic data of the patients diagnosed as H1N1 influenza

Demographic characteristics	No (%)
Residence	
Urban	141 (47.5)
Rural	156 (53.5)
Sex	
- male	148 (49.8)
pregnancy	1 (0.6% of females)
History of chronic medical condition	88 (29.6)
Asthma	9 (3.0)
Respiratory illness (COPD*)	13 (4.4)
Cardiovascular diseases	7 (2.4)
Neurologic disease (CVA,…)	11 (3.7)
Immune deficiency	2 (0.7)
Others	46 (15.5)
Age	Mean: 24.4±15.8
Occupation	
Student	103 (34.7%)
Housewife	58 (19.5%)
College or university student	17 (5.7)
Office employee	17 (5.7)
Health care worker	7 (2.4)
Others	95 (32.0)
History of travelling abroad (last 6 months)	32 (10.8)
History of contact with a person with flu-like illness in the last 6 months	101 (34)
Status:	
Outpatient	221 (74.4)
Hospitalized	76 (25.6)
Death	11 (3.7)
Medications prior to referral	
Tamiflu (Oseltamivir)	3 (1.0)
Antibiotics	15 (5.0)
Corticosteroids	3 (1.0)

•COPD: Chronic Obstructive Lung Disease

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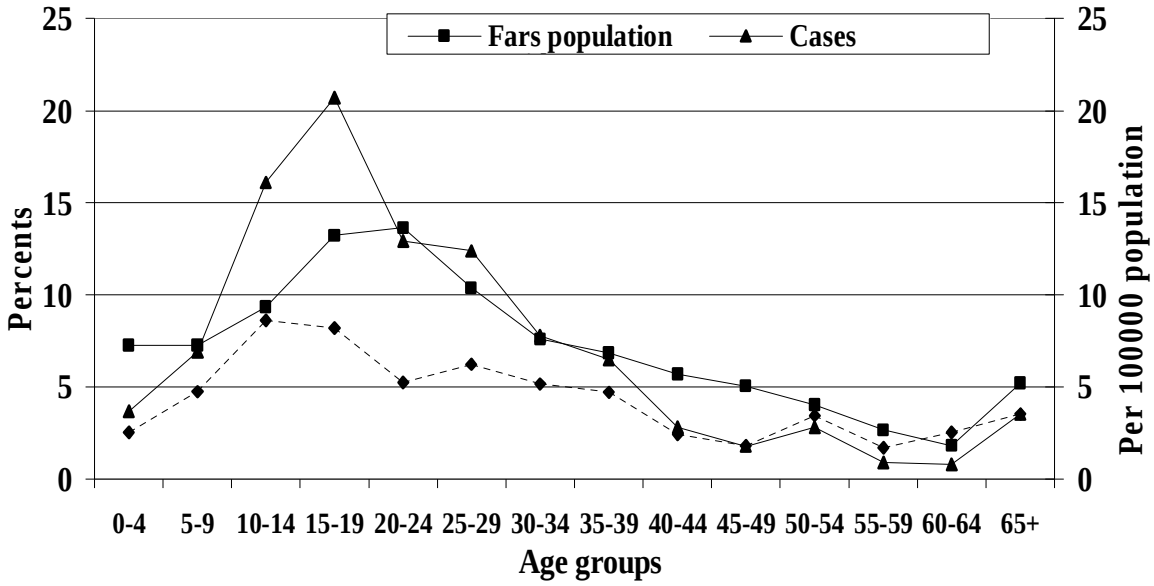

Fig. 1: Age distribution of 297 confirmed cases of Influenza A (H1N1) from Jul 15 to Dec 3 2009 compared with age distribution of Fars population, (dotted line (- - -♦- - --) shows incidence rate per 100000).

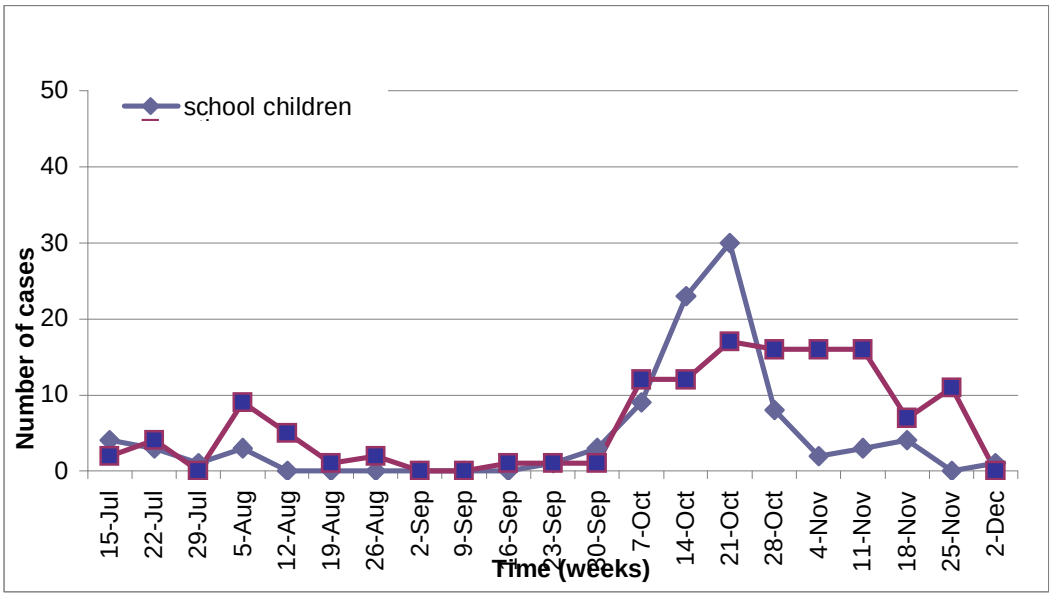

Fig. 2: Time distribution of confirmed cases of influenza A (H1N1) in students compared to other occupations from Jul 15 to Dec 3, 2009, Fars Province, South of Iran

mean age was 39.4±23.1 years which was significantly higher than that of the admitted or outpatient groups with no report of death (22.6±14.1) (p<0.001). Also, the value was significantly higher compared to the overall mean age of the patients (p<0.001). The highest incidence of the disease was observed in mid October 2009 after its emergence in the early July 2009 (Figure 3).

The number of new H1N1 flu cases steadily reduced from its peak on 14-27th of October 2009 and

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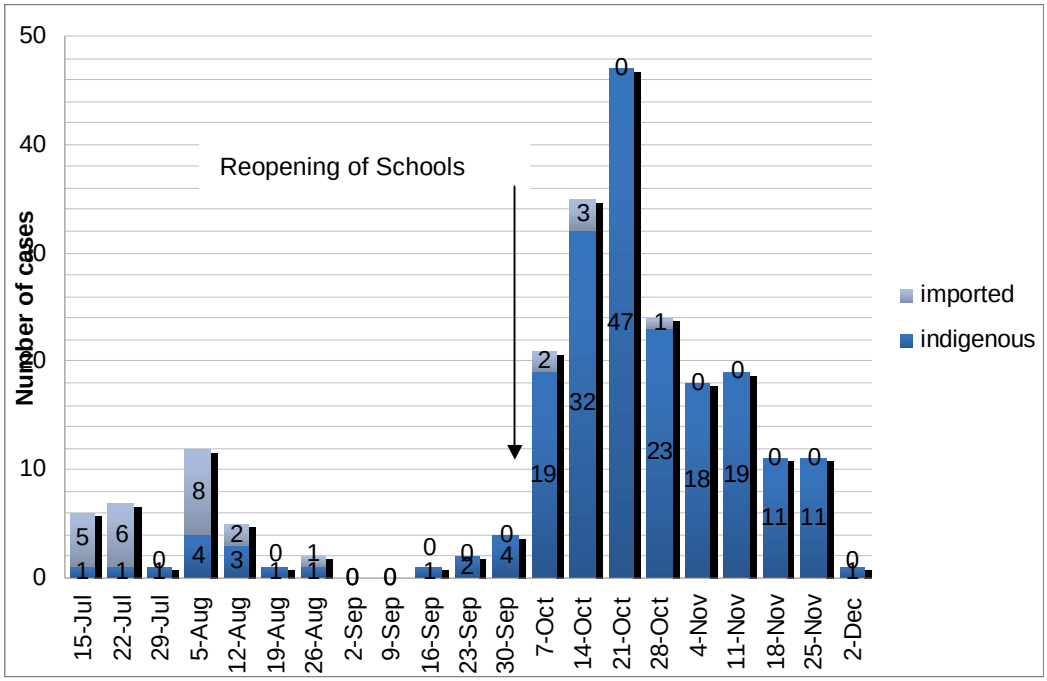

Fig. 3: Time distribution of 253 confirmed cases of Influenza A (H1N1) from Jul 15 to Dec 3, 2009, according to sources of infection, Fars Province, South of Iran. (by the time of this report the accurate data was available for 253 out of 297 patients)

the reduction continued up to the time we were preparing this report.

Regarding the concomitant medical illness of the subjects, 88 (29.6%) cases had a pre- existing health condition, the most frequent of which was respiratory illnesses (22 patients), 25% including asthma (9 cases), 3% of the study population and chronic obstructive pulmonary disease (13 cases), 4.4% of the study population. Among these, 27 patients were admitted in hospitals. Statistical analysis of the mortality rate and hospital admissions showed no significant difference between those with pre-existing health condition and the otherwise healthy individuals. (Hospitalization rate was 30.7% in those with medical conditions compared to 26.5% overall) (p>0.05). Of those who died due to H1N1 flu, only one patient had a chronic health condition and the rate of hospitalization was similar in both groups. The most common presenting symptoms of the individuals were fever (85.3%), cough (58.3%), sore throat (57.1%) and myalgia (48%). Overall, 95.4% of the cases presented with at least one of these symptoms (Figure 4). Moreover, the type of presenting symptoms and outcome of the patients (outpatient, hospitalized or dead) had no correlation.

Discussion

Since the declaration of H1N1 flu pandemics by WHO in April 2009, many countries have been affected by this pandemic and its burden. According to the available reports, this pandemic has had multiple waves in countries so far with the first wave mostly consisting of cases traveling from across the borders.[12-15] Fars province is located in the south of Iran with approximately 4,300,000 inhabitants and it is one of the major entrance gateways from nearby countries with almost 10,000 passengers weakly.[16] The first confirmed case of H1N1 influenza in Fars province was a 17 year old teenage boy who had developed flu-like illness symptoms after returning to Iran from overseas (USA) and the diagnosis was confirmed later by 15th of July 2009. The incidence pattern of the disease in Fars was the same as that in other parts of Iran. H1N1 pandemic occurred in Fars province with two main waves. The first wave of the disease was observed in mid July 2009 peaking at August with more than 66% of the cases consisting of those with a history of foreign travel (overseas source of infection). However, the incidence rates gradually reduced later in September. The second wave of the

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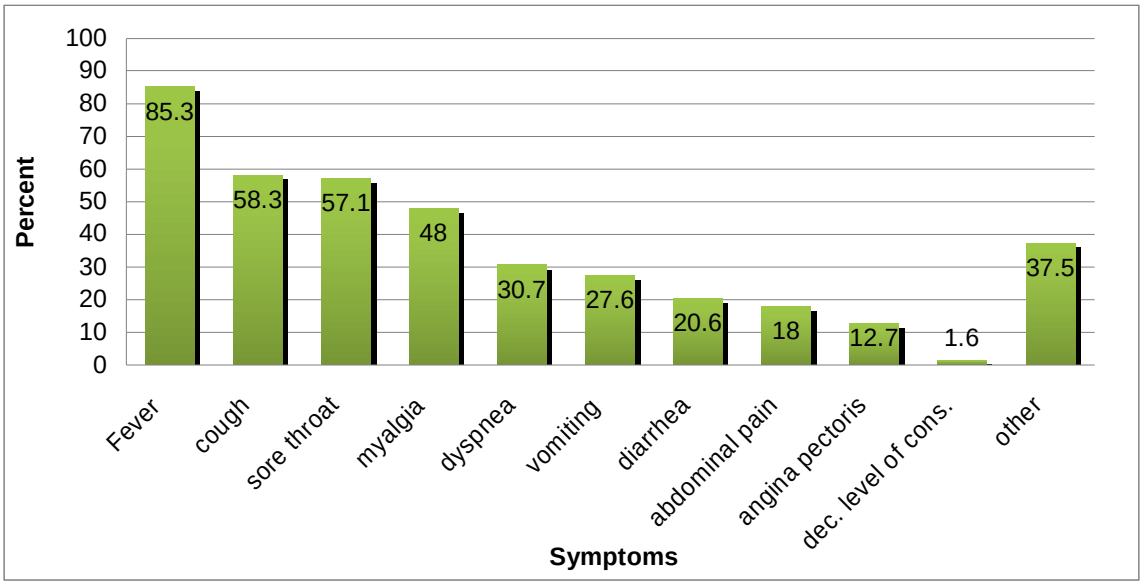

Fig. 4: Frequency of symptoms related to H1N1 influenza in the community

disease started in the first week of October and peaked in the next 2 weeks (Figure 3).

Schools re-open in the first week of October each year and this was in concordance with the start of the second wave of the disease which highlights the effect of close contacts of students with each other and its role on spread of the H1N1 flu. This is confirmed by the fact that 103 (41%) of all confirmed cases were students and unlike the first wave of the disease, the second one mostly included cases who had been affected inside the country and were not related with foreign travel. (Indigenous source) Moreover, the magnitude of the epidemic was also much higher in the second wave, when the disease was transmitted between students and then by them in their families. As students have a closer contact with each other and each of them is a member of a family, it seems that preventive measures should be more focused on this population during such epidemics. Increasing the students' knowledge regarding the means of transmission will prevent the dissemination of the disease in the families and the community. Hence, preventive measures have been taken by health care system in order to increase people's awareness in the society. Interestingly, the incidence of H1N1 flu has been decreasing since late October following the execution of these plans. The policies that have been implemented in our country since the start of the pandemics such as school closures in the case of certain circumstances and educating the society about preventive measures played a significant role in decreasing its incidence as with the same experience in other countries.[17-22]

Observation of an approximately 70% decrease in occurrence of new cases in the 4th week of November compared to the peak of the second wave in October supports the efficacy of these strategies.

On the other hand, there have been efforts on the way to provide a thorough and effective vaccination program in the country. The current worldwide guidelines for pandemic flu vaccination have focused on children from 6 months to 18 years and pregnant women as target groups for vaccination.[23,24] Due to the high prevalence of H1N1 influenza in children of school age, targeting this age group for vaccination can contribute to better control of this pandemic in our society.

Our results regarding distribution of the incidence of H1N1 influenza based on sex or occupation didn't show any significant difference in different groups. The distribution of the disease based on age was similar to that of other studies and most patients were in the age group 5-15 years.[25,26] Patients with chronic health conditions especially lung diseases are considered to be at higher risk for complications and mortality due to pandemic flu;[27,28] yet, our analysis revealed no significant correlation between the pre-existing medical condition of the patients and the severity of symptoms or rate of hospitalization or mortality. A

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study in Argentina revealed that 35% of their H1N1 cases suffered from a chronic medical condition[28] while the value in our study sample was 29.6%.

Similar to the results of the mentioned investigations, asthma was identified as the most frequent underlying condition in both hospitalized and outpatient H1N1 influenza cases in our survey. However, the overall prevalence of underlying medical condition among those hospitalized as H1N1 influenza cases was significantly lower than that in other studies. (35.5% compared to 73% in USA) The same investigation revealed that 68% of their mortality cases suffered from a chronic health condition while only one (9%) of the 11 cases who died had an accompanying medical condition in our investigation.[27] The only case of mortality was an 80 year old man with a history of heart failure. Our findings are in contradiction with worldwide reports that attribute 60% of the fatal cases to comorbid health conditions.[29,30]

This comparison highlights the lower mortality and morbidity of H1N1 influenza in our population (in either otherwise healthy individuals or those with chronic diseases).

Using available diagnostic tests, we found that the total number of cases would be about 151505 and the number of severe cases who needed to be hospitalized was estimated to be 683.[31] But the reported cases and hospitalized numbers are much less based on the available local and national reports.

We have previously discussed the possible theories behind this low rate of hospitalizations or mortality in our community which might be some kind of pre-existing immunity in our individuals or high rate of asymptomatic infections in our country.[32]

Yet, there are limitations to our conclusions, the most important of which being the fact that we are suffering from under-reporting of the disease. The surveillance system, although effective, might not be able to report all cases of H1N1 influenza in our society. Another issue is that not all patients with flu-like illness symptoms refer to specialized centers for H1N1 flu evaluation and this can affect our results regarding the true prevalence of this disease in our society. In fact, since symptoms and signs of H1N1 influenza are similar to other viral respiratory diseases, physicians might not be able to differentiate them from each other. For instance, prescription of corticosteroids at first visit leads to suppression of symptoms and therefore fewer suspicious cases are referred to flu centers for definite diagnosis. Overall, the mentioned issues contribute to under- reporting of H1N1 influenza. Therefore, larger ongoing studies are needed to provide a better understanding of the true prevalence or incidence of H1N1 influenza in our region.

Conflict of interest: None declared.

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