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Investigation of the Relationship Between Demographic Characteristics and Frequency of Mortality in Certain Cases of Influenza A (H1N1) From Yazd Province (Iran)

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Background: One important feature of influenza viruses is the high rate of mutation in the virus coat proteins, hemagglutinin and neuraminidase. These viruses are related to RNA viruses and belong to the family *Orthomyxoviridae*. Virus antigenic variations are called antigenic drift or minor changes and antigenic shift or widespread changes. The large pandemic of influenza is usually caused by virus antigenic shift. A new form of the influenza virus is called influenza virus A (H1N1).
Objectives: The purpose of our study was to investigation of the relationship between demographic characteristics and frequency of mortality in certain cases of influenza A (H1N1) from the Yazd Province of Iran.
Materials and Methods: We referred to a health center of the Yazd province to collect characteristics and information related to patients during years2008 – 2009. This study was descriptive and analytical. Out of 1442 patients suspected of influenza during the study period, 253 throat samples had positive with RT-PCR (reverse transcriptase-polymerase chain reaction) results, which were confirmed for viruses. After obtaining the names and contact numbers of these patients, their information and data were recorded in the Excel program and then were analyzed using the SPSS software and chi-square statistical method.
Results: Out of 253 cases confirmed for influenza A (H1N1), 9 women and 11men had died. Amongst these cases the minimum and maximum age was3.5 and90 years, respectively. Also, from the 20 confirmed cases of influenza A (H1N1) that had died, 16 cases had at least one underlying disease.
Conclusions: There was no significant association between mortality of confirmed cases of influenza A (H1N1) and sex, but the results demonstrated that mortality may be associated with age and underlying diseases.

Keywords: Influenza A (H1N1); Mortality; Demographic

1. Background

Influenza, commonly referred to as the flu, is an infectious disease caused by RNA viruses of the *Orthomyxoviridae* (the influenza viruses). Influenza A virus causes it and is the only species of influenza virus A. Influenza A viruses are negative sense, single-stranded, segmented RNA viruses. There are several subtypes, labeled according to an H number (for the type of hemagglutinin) and an N number (for the type of neuraminidase) (1, 2). The influenza virus is a highly contagious virus that causes acute respiratory disease. Usually, influenza causes pneumonia which can be fatal in young patients or people with immunodeficiency. In addition, influenza is spread in seasonal epidemics throughout the world and kills countless people in pandemic years (3).

Influenza A and B viruses are responsible for the vast majority of the 200000 to 500000 deaths and billions of US dollars in economic losses attributed to annual infections globally (4, 5). The impact of factors such as age, sex and disease, on how individuals fight pathogens, lead to differences in the rate of occurrence, duration and severity of infections and diseases, particularly influenza (6). In developed countries, such as the United States of America and Spain, the reported incidence of seasonal influenza virus infection is higher for males (up to 60% in the United States) than females of diverse ages, ranging from infants to elderly adults (7).

Virus symptoms include upper respiratory system dis-

Implication for health policy/practice/research/medical education:
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eases such as sinusitis and otitis media, lower respiratory tract illnesses such as bronchitis, toxic shock syndrome, etc (8). Typical clinical manifestations include fever, headache, cough, sore throat, myalgia as, chills, and fatigue. Diarrhea and vomiting may also occur (9). Useful laboratory methods for diagnosis are RAT (Rapid Antigen Test) and RT-PCR (reverse-transcription polymerase chain reaction). RT-PCR is an optional test and has 98% sensitivity (10). Antiviral drugs such as oseltamivir (Tamiflu) and zanamivir (Relenza) are effective against both influenza A and B (11).

Studies have shown that a single dose of influenza vaccine A (H1N1) will increase safety, especially for elderly (12-17). In April 2009, the first case of influenza A H1N1 was registered in Mexico and lead to an unexpected number of deaths. This study reported the timing and spread of H1N1, and explored the protective and risk factors for infection, severe disease, and death. 63,479 cases of influenza-like illness were reported, from which 63 cases died (18). When the 2009 H1N1 influenza A virus emerged in the United States, epidemiological and clinical information about severe and fatal cases was limited. One study reported the first 47 fatal cases of 2009 H1N1 influenza in New York City. In this study, which took place from the 24^{th} of April to the 1st of July 2009, 47 confirmed fatal cases of 2009 H1N1 influenza were reported to the New York City Department of Health and Mental Hygiene. Most decedents were aged between 18–49 years, and only 4% were aged up to 65 years (19).

In another study Influenza-associated excess mortality for the period between 2003-2008 was estimated for three cities in temperate northern China and five cities in the subtropical south of the country. Most (86%) deaths occurred among people aged ≥ 65 years (20). In another study Influenza A co infections with other respiratory viruses were investigated in 25.8% of the samples from patients hospitalized in 2009 at a hospital in Brazil. In this study co infection was not associated with higher morbidity or mortality (21).

2. Objectives

In accordance with the above findings, the present study was performed to investigate the relationship between demographic characteristics and frequency of mortality in certain cases of influenza A (H1N1) in Yazd Province during years 2008 – 2009.

3. Materials and Methods

In this cross sectional study, sampling was carried out as a census of all influenza patients. Information related to about 1442 patients with suspected influenza A (H1N1) from the Yazd province, for years 2008 – 2009, was available at the Health Center; these data were related to appropriate throat samples. These samples were taken from patients at admission or outpatient visit to each of the hospital or emergency centers in the province cities. Samples were sent to the Kerman reference laboratory. In the reference laboratory RT-PCR was per formed and results were submitted to the Health Center of the Yazd province. We used these results for our research.

Personal information related to patients in a linear list include: name, address, sex, age, occupation, nationality, residence, travel history (outside or inside the country) during the previous ten days, last dose of influenza and pneumococcal vaccination, history of contact with influenza patients or animals during the previous ten days, date of initial symptoms, date of sample gathering and sending, condition of the patient (admission or outpatient),most obvious signs of disease, report date and phone number. Finally 253 cases of confirmed influenza were identified.

For completing records related to cases for which underlying disease was not mentioned, we phoned them and if they were not available, because of being very young or very old, information was obtained from the individual who was closest and had the most knowledge about the patient. Results were recorded in the Excel software and analyzed using the SPSS software and chi-square statistical method.

4. Results

After investigating available records from the Health Center of Yazd province, information related to 253 patients with confirmed influenza A (H1N1) for years2008 – 2009 were recorded in the Excel program and analyzed using the SPSS software and chi-square statistical method. In this study results were as follows:

4.1. Frequency of Mortality of Influenza A (H1N1) Confirmed Cases Based on Gender

Out of the 253 confirmed cases infected with the disease, 20 mortality cases had been reported. Ofthese, 9 cases (7.3%) were women and 11 cases (6.3%) men. A significant correlation was no found between mortality and sex ($P = 0.76$) (Table 1).

Table 1. Frequency of Mortality of Influenza A (H1N1) Confirmed Cases Based on Gender

Death Report	Not Dead, No. (%)	Dead, No. (%)	Total, No. (%)
Gender			
Female	102 (92.7)	9 (7.3)	111 (100)
Male	131 (93.7)	11 (6.3)	142 (100)

4.2. Frequency of Mortality of Influenza A (H1N1) Confirmed Cases Based on Age

Out of the 20 deaths that were reported, the youngest patient was 3.5 years old and the oldest patient was 90

years old. Mortality was not reported for the age group of 14-5 years. In this part of the study a significant correlation between mortality and age was observed (P = 0.001) (Table 2).

Table 2. Frequency of Mortality of Influenza A (H1N1) Confirmed Cases Based on Age

Mortality Cases	<60 , No. (%)	30-59, No. (%)	15-29, No. (%)	5-14, No. (%)	0-4, No. (%)
Dead	13 (26.6)	5 (7.4)	1 (1.5)	0 (0)	1 (8.3)
Not Dead	36 (73.4)	63 (92.6)	65 (98.5)	58 (100)	11 (91.7)
Total	49 (100)	68 (100)	66 (100)	58(100)	12 (100)

Frequency of mortality of influenza A (H1N1) confirmed cases based on underlying diseases Out of the 20 confirmed deaths, 16 cases (17.2%) had at least one underlying disease (Table 3).

Table 3. Frequency of Mortality of Influenza A (H1N1) Confirmed Cases Based on Underlying Diseases

Underlying Disease Mortality	P = 0.001, No (%)	With Underlying Disease, No (%)	Lack of Underlying Disease, No (%)
Dead	20 (8.3)	16 (17.2)	4 (2.7)
Not Dead	219 (91.7)	81 (82.8)	138(97.3)
Total	239 (100)	97 (100)	142 (100)

Out of the 16 dead patients with underlying disease, 7 cases had pulmonary chronic disease. This underlying disease had a significant correlation with mortality (P = 0.001). 6 patients suffered from diabetes and there was a significant correlation between these cases and mortality (P = 0.008). 5 patients had hypertension and there was a significant correlation between these cases and mortality (P = 0.079). Also a significant correlation was found between chronic heart disease, malignancies and mortality, with P values of 0.05 and P = 0.001, respectively.

In this study a significant correlation was not found between renal disease (P = 0.92), asthma (P = 0.347), blood diseases (P = 0.457), immune deficiency diseases (P = 0.542) and mortality. Also in this study mental retardation, cerebral stroke and pregnancy were not mortality cases (Table 4). We used chi-square statistical method for the above cases.

Table 4. Frequency of Underlying Diseases in Confirmed Mortality Cases of Influenza A (H1N1)

Underlying Disease	P Value	Confirmed Cases of Influenza A (H1N1), No. (%)	Confirmed Mortality Cases of Influenza A (H1N1) , No (%)	Total
Chronic Lung Disease	0.001	13 (65)	7 (35)	20 (100)
Diabetes	0.008	22 (78.6)	6 (21.4)	28 (100)
Hypertension	0.079	25 (83.3)	5 (16.7)	30 (100)
Heart Disease	0.050	16 (80)	4 (20)	20 (100)
Malignancies	0.001	4 (50)	4 (50)	8 (100)
Asthma	0.347	11 (84.6)	2 (15.4)	13 (100)
Kidney Disease	0.928	12 (92.3)	1 (7.7)	13 (100)
Pregnancy	0.492	6 (100)	0 (0)	6 (100)
Blood Diseases	0.457	5 (83.3)	1 (16. 7)	6 (100)
Immunodeficiency Diseases	0.542	3 (75)	1 (25)	4 (100)
Mentally Retarded	0.694	2 (100)	0 (0)	2 (100)
Cerebral Stroke	0.782	1 (100)	0 (0)	1 (100)

5. Discussion

Human influenza is a self-limiting disease. Global pandemics of influenza A (H1N1) is an event that may suddenly happen. This event will cause referral of a very large population of patients to health centers. This study was performed to investigate the relationship between demographic characteristics and frequency of mortality in certain cases of influenza A (H1N1)in Yazd Province in Iran. In April 2009, the first case of influenza A H1N1 was registered in Mexico and was associated with an unexpected number of deaths. This study reported the timing and spread of H1N1, and explored protective and risk factors for infection, severe disease, and death. 63,479 cases of influenza-like illness were reported; 6945 (11%) cases of

H1N1 were confirmed, 6407 (92%) were outpatients, 475 (7%) were admitted and survived, and 63 (<1%) died. Those aged between 10-39 years were most affected (3922 [56%]). Mortality rates showed a J-shaped curve, with greatest risk in those aged 70 years and older (10·3%). Delayed admission and presence of chronic diseases were associated with increased risk of death. This study was very similar to the present study except that in the present study, the dead cases were 7.9% of the total (18).

Another report studied the 2009 H1N1 influenza A virus emergence in the United States for which epidemiological and clinical information about severe and fatal cases was limited. This study, reported on the first 47 fatal cases of 2009 H1N1 influenza in New York City. Most decedents (60%) were aged 18–49 years, and only 4% were aged > 65 years. Many (79%) had underlying risk conditions for severe seasonal influenza, and 58% were obese according to their body mass index. Thirteen (28%) had evidence of invasive bacterial co infection. Approximately 50% of the decedents had developed acute respiratory distress syndrome (19). Comparison of this study with the present study showed that in the present study, most cases of death were related to the age group of > 60 years and 80% of mortality cases had at least one underlying disease, which suggests that underlying diseases are important in influenza A virus pandemics.

In another study, influenza-associated excess mortality for the period of 2003-2008 was estimated in three cities in temperate northern China and five cities in the subtropical south of this country. Annual influenza-associated excess mortality, for all causes, was 18.0 (range: 10.9–32.7) deaths per 100,000 people in the northern cities and 11.3 (range: 7.3–17.8) deaths per 100,000 in the southern cities. Excess mortality from respiratory and circulatory disease was 12.4 (range: 7.4–22.2) and 8.8 (range: 5.5–13.6) deaths per 100,000 people in the northern and southern cities, respectively. Most (86%) deaths occurred among people aged ≥ 65 years (20). Comparison of this study with the present study reveals similarity, in that in the present study most cases of death were also from the age group of > 60 years.

Furthermore, a study on influenza A co infection with other respiratory viruses, investigated 25.8% (41/159) of the samples from patients hospitalized in 2009 at a hospital in Brazil. Out of the 41 influenza A cases, nine cases (21.9%) were co infected with other viruses, with a similar frequency among children and adults (P = 0.47), and seasonal influenza cases were more prevalent than H1N1 2009 influenza virus. Adenovirus was the most frequently detected (4/9) among co infected cases. Co infection was not associated with higher morbidity or mortality (P = 0.75) (21).The difference between this study and the present study is that in our study a significant correlation between mortality of influenza A (H1N1) confirmed cases and underlying diseases, was evident.

In accordance with the above studies, an investigation of the relationship between demographic characteristics and frequency of mortality in certain cases of influenza A (H1N1) is essential; something that the present study has tried to address.

It is concluded from the study that:

1. Due to the high mortality of the older group and people who have underlying diseases, the prevention of influenza A (H1N1) and its rapid treatment can reduce mortality in these cases.

2. Due to the high rate of mortality from influenza A (H1N1) in people with l ung chronic diseases, it is essential to pay particular attention to these people compared to other groups.

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Authors Contributions

None declared.

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