

*Original article*

# Epidemiology of Influenza in Patients with Acute Lower Respiratory Tract Infection in South of Iran (2015-2016)

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## SUMMARY

Influenza is of particular importance because of the pace of epidemics, the extent and number of infected people, and the severity of the side effects. The aim of this study was to investigate the epidemiological and clinical aspects of this disease during the last epidemic in southern Iran.

The present cross-sectional study was performed on the basis of secondary data analysis and information in medical records of patients with acute lower respiratory system infection in hospitals affiliated to Jahrom University of Medical Sciences. Data were analyzed by SPSS 18 using descriptive statistics, Chi-square test and logistic regression at 0.05 significance level.

From 1<sup>st</sup> September 2015 to 20<sup>th</sup> March 2016, 108 patients with acute lower respiratory tract infection with a mean age of  $42.92 \pm 19.65$  years were admitted to Jahrom hospitals, of which 43 were diagnosed with definite influenza, all of which (100%) had H1N1 type A influenza. There were eight deaths in all, of which five were positive for H1N1, and of these five cases, three cases had delayed diagnosis and treatment, and four cases had underlying diseases. The results of multivariate logistic regression analysis showed a significant relationship between positive H1N1 cases and history of contact with definite influenza, traveling abroad, and clinical symptoms of chills ( $p < 0.05$ ).

The results of this study showed that 39.81% of the patients with acute lower respiratory tract infections suffered from influenza. Furthermore, the delayed treatment and the underlying diseases were the most important cause of death.

**Key words:** influenza A Virus, epidemiology, H1N1 subtype

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## INTRODUCTION

Respiratory tract infections, which are associated with mortality and morbidity, are one of the most common infections and one of the most important reasons for hospitalization around the world (1). Childhood a topic disease and its comorbidities have been increasing in developed countries over the past few decades (2). Also, asthma exacerbations may be induced by respiratory viruses (3).

Upper respiratory tract infection (URTI) or “the common cold” is a symptom complex usually produced by several families of the virus: the rhinovirus, coronavirus, parainfluenza, respiratory syncytial virus (RSV), adenovirus, human metapneumovirus, and influenza (4).

Lower respiratory infections (LRTI) include pneumonia (infection of the lung alveoli) as well as infections affecting the airways such as acute bronchitis and bronchiolitis, influenza and whooping cough. They are the leading cause of illness and death in children and adults across the world (5). The Global Burden of Disease (GBD) project estimates that nearly 2 million of the 2.74 million LRTI-associated deaths were in adults  $\geq 70$  years and children  $< 5$  years old and that 10% were attributable to influenza (6). The relationship between severe influenza disease in adults and LRTI has been recognized for at least a century (7).

The influenza is an acute disease that affects the upper and lower respiratory tracts, and is often associated with systemic symptoms such as fever, myalgia, and weakness (8).

Due to the presence of other microbial agents in developing flu-like illnesses, the diagnostic decision based on epidemiological and clinical findings and the treatment of people at high risk of mortality should not be delayed until obtaining laboratory confirmation (9).

Type A influenza virus has been able to create epidemics and pandemics. On the other hand, type B influenza virus is less responsible for broad-based regional epidemics and type C influenza virus contributes to sporadic cases and limited epidemics (8).

The influenza virus has a genetic variability potential more than any other virus that uses these antigenic drift in a regular and predictable manner as an effective strategy against the obtained immunity, forcing us to produce annually various vaccines. Sometimes, they are so foreign to the human immune system because of the major antigenic changes (antigenic shift) and the lack of a previous immunization history, leading to a new pandemic (8, 10).

In the event of a new virus subtype, all children and adults are equally susceptible, except those who were immune to the subtype during the previous epidemics; the durability of this new subtype depends on the subsequent antigenic drift (11, 12).

One of the new type A viruses is the H1N1 subtype swine influenza virus, which is a variant of an asymptomatic and uncomplicated upper respiratory tract infection to the development of acute pneumonia with severe damage to other organs (13).

Fever, headache, body aches, fatigue, diarrhea, vomiting, and upper respiratory symptoms such as cough, runny nose, and sore throat are the most common clinical features of swine influenza (14). This subtype was responsible for a wide pandemic for the first time in 2009 during three months, causing death of 18,138 people around the world (15, 16).

In 2009 H1N1 influenza pandemic in Iran, 2,662 patients were diagnosed with definite H1N1 influenza from 1 June to 11 November, and 58 patients (2.18 %) died during this pandemic (17).

Furthermore, a new wave of influenza epidemic emerged in Iran in late autumn 2015, resulting in large numbers of hospitalization and deaths of dozens of people (Kerman, Rafsanjan, Sistan and Baluchestan). In Jahrom, the number of hospitalized patients increased due to acute respiratory infections suspected of influenza, which coincided with the return of Arba'een pilgrims from Iraq.

An analysis of the results of epidemiological surveillance systems of influenza epidemics in all countries is important in order to gain better understanding of the disease and its impact on the future interventions such as immunization. Therefore, the present study was conducted to determine the epidemiological and clinical aspects of influenza during the last epidemic of 2015 in Jahrom, Iran.

## MATERIAL AND METHODS

The present cross-sectional study was performed on the basis of secondary data analysis and information in medical records of patients with acute lower respiratory tract infection in hospitals affiliated to Jahrom University of Medical Sciences.

It should be noted that samples were examined on the basis of RT-PCR recommended by the United States and the WHO to detect and identify the H1N1 virus, and then the results were given to the sampling ward (18).

Data were analyzed using the SPSS Version 18.0. Chi square test, Odds Ratio (OR) and corresponding 95% confidence interval (% 95 C.I) were used to evaluate the relationship between independent variables and H1N1 status as a dependent variable. In order to control the effect of possible confounders, the adjusted ORs were estimated using the backward multiple logistic regression method. Statistical analysis was performed at 0.05 significance level. It should be noted that the Ethics Committee of the Deputy of Research at Jahrom University of Medical Sciences approved the research project with the ethics code of IR.jums.REC.1396.004.

## RESULTS

From 1<sup>st</sup> September 2015 to 20<sup>th</sup> March 2016, 108 patients with acute lower respiratory tract infection (51 women and 57 men) with a mean age of 42.92 ± 19.65 years and median of 42.5 (2-92 years) were admitted to Jahrom hospitals. In terms of distribution of occupational groups, the highest frequency was related to the self-employed (n = 43, 39.8%) and homemakers (n = 43, 38.9%). Among the patients, 34 (31.5%) had a history of

traveling abroad, and all of them had travelled to Iraq. Of all admitted patients, 22 (20.4%) had a history of contact with definite influenza (Table 1).

All (100%) samples were obtained from throat swab. According to Table 2, the flu-like cases were fever (n = 83, 76.9%), sore throat (n = 83, 76.9%), cough (n = 82, 75.9%) and muscle aches (n = 77, 71.3%). The consumed drugs were Oseltamivir in 98 (90.7%), Zanamivir in 8 (7.4%) and ceftriaxone combined with azithromycin in 2 (1.9%) subjects. From the influenza subtypes during the study period, out of 108 cases of recorded influenza-like diseases, 43 cases had definite influenza, and all (100%) of them had type A and subtype H1N1. Totally eight deaths occurred in subjects with the mean age of 43 ± 19.8 years, of which 5 cases were confirmed H1N1 and 3 cases were unconfirmed. The age group of 15-40-year olds had the highest incidence and mortality rate in confirmed H1N1 individuals and the unconfirmed group had the highest incidence in the age group of 40-65 years and the highest mortality rate in the age group over 65 years (Table 3). In addition, the highest incidence and mortality rates in confirmed H1N1 individuals were recorded in December (Graph 1).

**Table 1. The frequency of demographic variables in patients with acute lower respiratory tract infection caused by H1N1**

| Variables  | Levels        | All cases of acute respiratory tract infections |            | Unconfirmed H1N1 |            | Confirmed H1N1 |            | P-value* |
|--|---------------|---|------------|------------------|------------|----------------|------------|----------|
|  |               | Frequency                                       | Percentage | Frequency        | Percentage | Frequency      | Percentage |          |
| Gender   | Male          | 57  | 52.8       | 30               | 46.2       | 27             | 62.8       | 0.09     |
|  | Female        | 51  | 47.2       | 35               | 5.8        | 16             | 37.2       |          |
| Occupational level                                 | Homemaker     | 42  | 38.9       | 29               | 44.6       | 13             | 30.2       | 0.38     |
|  | Employee      | 6   | 5.6        | 3                | 4.6        | 3              | 7          |          |
|  | Student       | 12  | 11.1       | 6                | 9.2        | 6              | 14         |          |
|  | Child         | 5   | 4.6        | 1                | 1.5        | 1              | 2.2        |          |
|  | Self-employed | 43  | 39.8       | 23               | 35.3       | 20             | 46.5       |          |
| Travelling to Iraq                                 | Yes           | 34  | 31.5       | 12               | 18.5       | 22             | 51.2       | < 0.001  |
|  | No            | 74  | 68.5       | 53               | 81.5       | 21             | 48.8       |          |
| Residence  | Urban         | 72  | 66.7       | 41               | 63.1       | 31             | 72.1       | 0.33     |
|  | Rural         | 36  | 33.3       | 24               | 36.9       | 12             | 27.9       |          |
| History of contact with a definite cases influenza | Yes           | 22  | 20.4       | 5                | 7.7        | 17             | 39.5       | < 0.001  |
|  | No            | 86  | 79.6       | 60               | 92.3       | 26             | 60.5       |          |
| History of contact with birds                      | Yes           | 5   | 4.6        | 2                | 3.1        | 3              | 7          | 0.345    |
|  | No            | 103   | 95.4       | 63               | 96.9       | 40             | 93         |          |

(\* P-value of chi -square test)

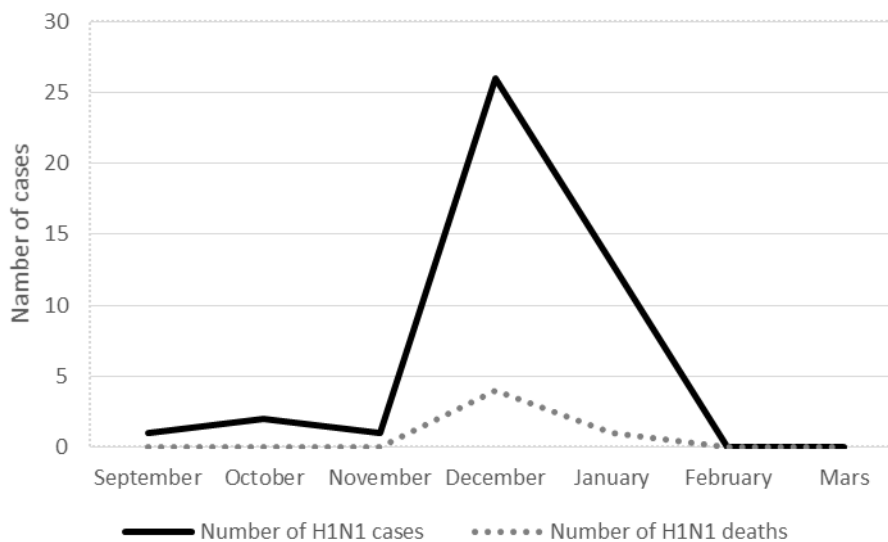
**Table 2. The frequency of clinical variables in patients with acute lower respiratory tract infection caused by H1N1**

| Variables                | Levels                  | All cases of acute respiratory tract infections |            | Unconfirmed H1N1 |            | Confirmed H1N1 |            | P-value* |
|--------------------------|-------------------------|---|------------|------------------|------------|----------------|------------|----------|
|                          |                         | Frequency                                       | Percentage | Frequency        | Percentage | Frequency      | Percentage |          |
| Fever                    | Yes                     | 83  | 76.9       | 46               | 70.8       | 37             | 86         | 0.06     |
|                          | No                      | 25  | 23.1       | 19               | 29.2       | 6              | 14         |          |
| Sore throat              | Yes                     | 83  | 76.9       | 47               | 72.3       | 36             | 83.7       | 0.16     |
|                          | No                      | 25  | 23.1       | 18               | 27.7       | 7              | 16.3       |          |
| Cough                    | Yes                     | 82  | 75.9       | 50               | 76.9       | 32             | 74.4       | 0.76     |
|                          | No                      | 26  | 24.1       | 15               | 23.1       | 11             | 25.6       |          |
| Chills                   | Yes                     | 27  | 28         | 8                | 12.3       | 19             | 44.2       | <0.001   |
|                          | No                      | 81  | 75         | 57               | 87.7       | 24             | 55.8       |          |
| Headache                 | Yes                     | 54  | 50         | 27               | 41.5       | 27             | 62.8       | 0.03     |
|                          | No                      | 54  | 50         | 38               | 58.5       | 16             | 37.2       |          |
| Diarrhea                 | Yes                     | 10  | 9.3        | 1                | 1.5        | 9              | 20.9       | 0.001    |
|                          | No                      | 98  | 90.7       | 64               | 98.5       | 34             | 79.1       |          |
| Vomit                    | Yes                     | 25  | 23.1       | 10               | 15.4       | 15             | 34.9       | 0.01     |
|                          | No                      | 83  | 76.9       | 55               | 84.6       | 28             | 65.1       |          |
| Muscle aches             | Yes                     | 77  | 71.3       | 42               | 64.6       | 34             | 81.4       | 0.04     |
|                          | No                      | 31  | 28.7       | 23               | 35.4       | 8              | 18.6       |          |
| Dizziness                | Yes                     | 25  | 23.14      | 13               | 20         | 12             | 27.9       | 0.34     |
|                          | No                      | 83  | 76.86      | 52               | 80         | 31             | 72.1       |          |
| Sneeze                   | Yes                     | 15  | 13.89      | 8                | 12.3       | 7              | 16.3       | 0.55     |
|                          | No                      | 93  | 86.11      | 57               | 87.7       | 36             | 83.7       |          |
| Coma                     | Yes                     | 8   | 7.4        | 3                | 4.6        | 5              | 11.16      | 0.173    |
|                          | No                      | 100   | 92.6       | 62               | 65.4       | 38             | 88.4       |          |
| Rhinorrhea               | Yes                     | 43  | 39.81      | 24               | 36.9       | 19             | 44.2       | 0.003    |
|                          | No                      | 65  | 60.19      | 41               | 63.1       | 24             | 55.8       |          |
| Dyspnea                  | Yes                     | 78  | 72.2       | 44               | 67.7       | 34             | 79.1       | 0.196    |
|                          | No                      | 30  | 27.8       | 21               | 32.3       | 9              | 20.9       |          |
| Underlying diseases      | Yes                     | 40  | 37         | 19               | 29.22      | 21             | 48.8       | 0.04     |
|                          | No                      | 68  | 63         | 46               | 70.78      | 22             | 51.2       |          |
| With underlying diseases | Cardiovascular          | 16  | 14.81      | 11               | 16.92      | 5              | 11.62      | 0.26     |
|                          | Nervous system diseases | 1   | 0.92       | 0                | 0          | 1              | 2.3        | 0.21     |
|                          | Chronic kidney disease  | 6   | 5.53       | 2                | 3.1        | 4              | 9.3        | 0.16     |
|                          | Diabetes                | 11  | 10.2       | 4                | 6.2        | 7              | 16.28      | 0.16     |
|                          | Pregnancy               | 5   | 4.62       | 1                | 1.5        | 4              | 9.3        | 0.06     |
| chronic liver disease    | 1                       | 0.92  | 1          | 1.5              | 0          | 0              | 0.41       |          |

(\* P-value of chi –square test)

**Table 3. Mortality percentage in each age group of confirmed H1N1 and unconfirmed cases with LRTI in southern Islamic Republic of Iran**

| Age                | Confirmed H1N1 |                | Unconfirmed H1N1 |                |
|--------------------|----------------|----------------|------------------|----------------|
|                    | Total (%)      | Death No. (%)* | Total            | Death No. (%)* |
| Under one year     | 0 (0)          | 0 (0)          | 0 (0)            | 0 (0)          |
| 1 – 5 years        | 0 (0)          | 0 (0)          | 2 ( 3.1)         | 0 (0)          |
| 5 – 15 years       | 1 (2.3)        | 1( 20)         | 4 ( 6.2)         | 0 (0)          |
| 15 – 40 years      | 21 ( 48.8)     | 3 (60)         | 25 (38.5)        | 0 (0)          |
| 40 – 65 years      | 17 (39.5)      | 1 (20)         | 22 (33.8)        | 0 (0)          |
| More than 65 years | 4 ( 9.3)       | 0 (0)          | 12 (18.5)        | 3 (100)        |



**Graph 1. The frequency of number of H1N1 cases and deaths based on the month of occurrence**

Of the five deaths of H1N1 influenza, there were three cases of delayed diagnosis and treatment (i.e. administration of the drug after 48 hours of the onset of symptoms) and four cases of underlying diseases. Of the total number of people with acute respiratory tract infection, five (4.6%) were pregnant. Finally, four of them were diagnosed with definite H1N1. Moreover, only two (1.9%) patients had a history of seasonal influenza vaccine before the disease, including one positive H1N1

and one negative H1N1.

The results of multivariate logistic regression analysis (Table 4) showed a significant relationship between H1N1 cases and history of contact with definite influenza (OR = 10.47, CI = 2.34-46.76), traveling abroad (OR = 6.27, CI = 2.00-19.62), and chills (OR = 5.66, CI = 1.63-19.6) ( $p < 0.05$ ).

**Table 4. The relationship between definite cases of influenza A (H1N1) virus infection and the study variables**

| Variables  | B     | OR    | OR (95%CI) | *P -value |
|--|-------|-------|------------|-----------|
| Gender   | 0.91  | 2.48  | 0.86-7.12  | 0.091     |
| History of travelling                                | 1.83  | 6.27  | 2.00-19.62 | 0.002     |
| Residence  | -0.12 | 0.82  | 0.28-2.7   | 0.82      |
| History of contact with a definite case of influenza | 2.34  | 10.47 | 2.34-46.76 | 0.002     |
| History of contact with birds                        | 1.33  | 3.78  | 0.35-40.53 | 0.27      |
| Fever  | 0.87  | 2.40  | 0.62-9.17  | 0.200     |
| Chills   | 1.73  | 5.66  | 1.63-19.60 | 0.006     |
| Vomit  | 0.43  | 1.53  | 0.41-5.75  | 0.52      |
| Muscle aches   | 1.03  | 2.81  | 0.59-13.34 | 0.19      |
| Underlying diseases                                  | 0.04  | 1.23  | 0.22-4.03  | 0.57      |

(\*Multivariate Logistic Regression Analysis)

## DISCUSSION

The acute lower respiratory tract infections affect a large number of people every year, and despite symptoms milder than influenza impose financial burden on the community, including being absent from work and pharmaceutical costs for their symptomatic treatment (19).

The results of the present study showed that 39.81% of the patients with acute lower respiratory tract infections suffered from influenza.

In 2009 H1N1 influenza pandemic in Iran, 2,662 patients were diagnosed with definite H1N1 influenza from 1 June to 11 November, of which 1,307 were women and 75% were cases in the age group of 5 to 40 years; 58 patients (18.2%) died during this pandemic. Furthermore, since 2009, influenza H1N1 cases have been reported sporadically from different regions of Iran.

The studies conducted in Khuzestan, Hamedan and Qazvin provinces of Iran showed that the per cent of patients with acute respiratory symptoms who were infected with influenza H1N1 was 19.1%, 12.62%, and 14.67%, respectively (20-22). These differences compared to the present study can be attributed to the establishment of a syndromic surveillance system for influenza in Iran in recent years after the widespread pandemics of influenza in 2009 and before. The syndromic surveil-

lance system is an organized data collection system that analyzes, interprets, and publishes public health information, whose goal is to achieve early diagnosis, health threats and rapid alert based on data obtained for preventing and controlling the outbreak of diseases in the community and promoting the responsiveness of the health system. In fact, all of the cases that occur in a small hospital or the neighborhood, and are not reported in the conventional care system, can be identified, recorded and reported within a few minutes in the syndromic form whose main function is to report and record the disease using hallmarks.

Traveling abroad is one of the effective factors in the outbreak of influenza. In a study conducted by Azizi, it was claimed that the pandemic of influenza entered Iran in 1918 from France (23). By studying the pandemic H1N1 influenza, Gooya et al. (17) in Iran pointed to the travel of about 120 thousand Iranians abroad annually. They estimated that about 20-30 thousand of these travels were because of the Umrah (Muslims' annual visit to Mecca) and travel to Saudi Arabia. In that year, the frequency of people with influenza-like syndrome was much higher in those who had a history of traveling because of the Umrah compared to those who had no such experience (17).

In this study, about 51.2% of people with H1N1 influenza had a history of traveling to Iraq during the Arba'een Pilgrimage. In fact, according to regression analysis, those who had a history of traveling abroad

were 6.27 times more likely to be infected with the disease compared to those who had no such history. Moreover, in a study in Hamadan province, Iran in 2013-2014, about 14% of people with respiratory illness had a history of traveling abroad, especially to Saudi Arabia and Iraq (24).

The incidence of symptoms in people with influenza-like illness is different in people and various ratios have been reported in different studies. In a study by Patricia et al., the incidence of cough was 59.6%, fever 11.3%, and sore throat 25% (25).

In the present study, history of chills, headache, diarrhea, vomiting, and muscle aches were significantly different in H1N1-positive and H1N1-negative patients ( $p < 0.05$ ). In a study conducted in Kurdistan, Iran, there was a significant difference in the signs of fever and muscle aches between H1N1-positive and H1N1-negative patients ( $p < 0.05$ ) (26). This difference in the incidence of symptoms can be due to the difference in the type of causative agents, gender ratio, age, vaccinated people ratio, and the study areas.

In the present study, the history of contact with a definite case of influenza was significant in H1N1-positive and H1N1-negative patients ( $p < 0.05$ ). People who had a history of contact with a definite influenza were 10.47 times more likely to be infected than those who did not. This finding is in line with the results of the study in Kurdistan on pandemics in 2009 as those with a history of contact were 2.92 times more likely to develop influenza ( $p < 0.05$ ) (26).

In three out of five deaths of H1N1 influenza, delayed treatment was the cause of death, which could be due to a lack of timely referral. This factor can be also seen in 9 out of 10 deaths in the 2009 pandemic in Markazi Province, Iran (27). In a study conducted in England during the 2009 flu pandemic in the United Kingdom, the most important cause of death was the delayed treatment, meaning drug administration after 48 hours of the onset of symptoms (28). Acute viral pneumonia is the most important cause of death in the influenza that leads to respiratory distress syndrome. The patients survived at this stage usually have the baseline underlying diseases including pregnancy, metabolic disorder, diabetes, people with weakened acquired immune system, and those who are being treated with immunosuppressants, malnutrition, obesity, and chronic pulmonary, heart and renal failures (29, 30). The results showed that 4 out of 5 deaths of H1N1 influenza were due to the history of underlying diseases (diabetes and cardiovascular diseases).

In the present study, the highest mortality rate was observed in adults, which is consistent with global

statistics. In most of the deaths, the delayed antiviral treatment was recorded as the main cause of death. In some patients, other causes for death have been also mentioned in the medical records, but the delayed antiviral treatment is the most important factor, indicating the importance of timely onset of drug administration in high-risk groups.

The drugs presently used include Oseltamivir and Zanamivir available from the beginning of the epidemic through government health centers and they are very effective medications for controlling symptoms and preventing the occurrence of deadly H1N1 influenza A and H5N1 influenza as long as no drug resistance occurs (31, 32).

As noted in the results, the antiviral drugs were available in all cases, and therefore the problem of the lack of antiviral drugs cannot be considered as the causes of death.

According to the results of the present study, despite the availability of seasonal influenza vaccine in public health centres and private pharmacies, only two (1.9%) had a history of seasonal influenza vaccination.

## CONCLUSION

The results of this study showed that 39.81% of the patients with acute lower respiratory tract infections were suffering from influenza. Furthermore, the delayed treatment and the underlying diseases were the most important cause of death. Therefore, early diagnosis and timely interventions are recommended for the treatment of this group of patients.

Due to the fact that pilgrims from this region travel to Iraq each year for pilgrimage to holy places, and especially the Arba'een Pilgrimage, they can be potent sources for the spread of the disease in the region. In this regard, the Ministry of Health and Medical Education should have more considerations for the seasonal influenza vaccination. Also, additional efforts should be made to ensure that the prevalent types and subtypes in the region are consistent with each type and subtype used in vaccines for preventive measures, as well as to obtain demographic information such as the history of traveling abroad, gender ratio and occupational status in identifying high-risk groups for vaccination.

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### **Conflict of interests**

The authors declare that there is no conflict of interest.



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## Epidemiologija gripa kod bolesnika sa akutnom infekcijom donjeg respiratornog trakta na teritoriji južnog Irana

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### SAŽETAK

Ispitivanje gripa ima poseban značaj zbog brzine razvoja epidemije, broja inficiranih osoba i težine sporednih efekata. Cilj ove studije bio je ispitivanje epidemioloških i kliničkih aspekata ove bolesti za vreme poslednje epidemije zabeležene u južnom Iranu.

Ova studija preseka urađena je na osnovu analize sekundarnih podataka i podataka iz medicinskih kartona bolesnika sa akutnom infekcijom donjeg respiratornog trakta u bolnicama koje su nastavne baze Univerziteta medicinskih nauka u Jahromu. Podaci su analizirani korišćenjem statističkog programa SPSS 18, kao i primenom Chi-square i logističke regresione analize sa nivoom značajnosti od 0,05.

U periodu od 1. septembra 2015. godine do 20. marta 2016. godine, u bolnici u Jahromu primljeno je 108 bolesnika sa akutnom infekcijom donjeg respiratornog trakta, čiji je prosek starosti iznosio od  $42,92 \pm 19,65$  godina; od ovog broja bolesnika, kod 43 bolesnika je dijagnostikovano grip i svi bolesnici (100%) su imali grip tipa A H1N1. Ukupno je zabeleženo osam smrtnih slučajeva, među kojima je pet osoba bilo pozitivno na H1N1, a od ovih pet slučajeva je kod tri osobe kasno uspostavljena dijagnoza, a samim tim i lečenje, dok su četiri osobe imale udružene bolesti. Rezultati multivarijantne analize pokazali su značajan odnos između slučajeva pozitivnih na H1N1 i istorije kontakata sa osobama zaraženim gripom, putovanja u inostranstvo i kliničkih simptoma prehlade ( $p < 0,05$ ).

Rezultati ove studije su pokazali da je 39,81% bolesnika sa akutnom infekcijom donjeg respiratornog trakta obolelo od gripa. Štaviše, zakasnelo lečenje i udružene bolesti bile su najznačajniji uzrok smrtnosti.

*Ključne reči:* virus gripa A, epidemiologija, H1N1 podtip