Int J Infect. 2021 October; 8(4):e116795. doi: 10.5812/iji.116795.

Published online 2021 October 16. **Research Article**

Epidemiology and Clinical Outcomes of Patients with Confirmed Influenza in Mashhad, Iran in 2019

Ashraf Tavanaee-Sani [1], Roshanak Sharifi [2,*], Zahra Nehbandani [3], Mohammad-Hasan Masoudi [3] and Yasaman Solouki [4]

[1] Department of Infectious Diseases and Tropical Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
[2] School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
[3] Deputy of Health, Mashhad University of Medical Sciences, Mashhad, Iran
[4] School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran

[*] *Corresponding author*: School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran. Email: sharifir941@mums.ac.ir

Received 2021 June 13; **Revised** 2021 September 25; **Accepted** 2021 September 28.

Abstract

Background: Influenza is a contagious and acute viral disease caused by influenza viruses involving upper and lower respiratory tract system, especially in the cold seasons. Children aged less than 5 years old, elderly people, immunocompromised patients, pregnant women, and people with certain health conditions are at a higher risk for the disease and severe complications.
Objectives: Due to the serious complications of influenza in certain groups, it is important to know which group of people are more at risk and need prevention strategies. This study aimed to investigate the patients with confirmed influenza, identify the people who are at a higher risk for infection, and assess the clinical outcomes of disease among patients.
Methods: In this cross-sectional and descriptive study, we studied the files of all patients with confirmed influenza referred to the health centers in Mashhad, Iran, during autumn and winter of 2019 when influenza virus was prevalent. The disease was confirmed by reverse transcription polymerase chain reaction (RT-PCR) method. We studied all registered data related to the flu, including gender, age, residency, history of vaccination, risk factors, complications, and clinical outcomes.
Results: In this study, 2977 patients (3% outpatients vs. 97% hospitalized) with flu like syndrome were tested by RT-PCR for influenza. Out of 84 outpatients, only two cases were positive for influenza. Among hospitalized patients, 80 cases (51% male vs. 49% female; age range: 1 - 87 years) had a positive RT-PCR test, and influenza type A was seen in 95% of cases. Pneumonia was the most common complication. Death happened in 29 (35.36%) patients and three (33.33%) cases with risk factors. The highest number of influenza patients (31 [37.8%]) had been reported from district No. 3 of Mashhad municipality, which is a crowded place and near the holy shrine.
Conclusions: The results showed a high prevalence of complication and death among hospitalized patients, especially among those who did not have a risk factor for influenza viruses. Comprehensive vaccination programs and promotion of knowledge about transmission routes are two important measures for disease prevention and lower death rates.

Keywords: Influenza, Clinical Outcome, Risk Factor

1. Background

Influenza is an acute infectious disease occurring in sporadic, outbreak, epidemic, and pandemic forms. Type A and B influenza viruses are responsible for the most cases of human illness (1, 2). While type A is related to widespread epidemics and pandemic forms, type B usually leads to sporadic and sometimes epidemic forms. Although all age groups can be infected with influenza virus, children younger than five years old, people older than 60, patients with chronic medical conditions (chronic kidney disease, chronic cardio-pulmonary diseases, and diabetes), pregnant women, and immunocompromised patients are at the highest risk of complications (1-5). In temperate climates, epidemics of the influenza virus occur more in the winter, but in tropical countries, the epidemic can occur throughout the year. It is estimated that these epidemics can lead to about 3-5 million cases of severe disease with serious complications and up to 550 thousand deaths around the world. Droplet nuclei (1 - 4 microns in diameter) remain suspended in the air, and inhalation of droplets situate the viruses in the upper and lower respiratory tracts, finally leading to pneumonia (1, 3-10). Treatment is usually supportive in mild forms, but in patients with severe infection and in those with certain risk factors

and chronic medical condition, anti-viral drugs such as rimantadine, amantadine, oseltamivir, and zanamivir can be effective (1-16). Periodically, changing in two viral glycoproteins located in the surface of virus named hemagglutinin (HA) and neuraminidase (NA) can lead to epidemic or pandemic forms of the disease. The results of such periodic changes are antigenic mutants, including antigenic drift of the virus (minor changes) and antigenic shift (major changes). Mutation can occur in one or both surface antigens (HA or NA), and more in the type A of influenza virus. Major changes lead to pandemic of influenza virus (2, 3, 12-18). There are many reports about epidemiology, clinical outcomes, and molecular variation of virus in Iran and worldwide (7-32). Since many contradictory results have been reported in studies about influenza in Iran, it seems that more attention should be paid to such factors as population size, gender, occupation, and underlying conditions. To date, the prevalence of influenza viruses including H3N2, H1N1, and B has not been evaluated well in Iran.

2. Objectives

We aimed to define the epidemiology of influenza in patients who had a positive RT-PCR test and had been registered in the Center of National Surveillance System for Influenza in Mashhad, Iran, in 2019. Meanwhile, we evaluated the rate of disease in patients according to age, sex, residency, risk factors (chronic kidney disease, chronic cardio-pulmonary diseases, diabetes, immunocompromised patients, pregnant women, etc.), vaccination history, complication rate, and clinical outcomes.

3. Methods

3.1. Study Design

In this cross-sectional and descriptive study, we evaluated the files of all patients with confirmed influenza (outpatients vs. hospitalized) referred to the Surveillance System for Influenza in Mashhad, Iran, during autumn and winter of 2019, when influenza virus was prevalent.

3.1.1. Study Area

Razavi Khorasan is a province located in northeastern Iran. Iran's "National Surveillance System for Influenza" was established in 2004. According to strategies in this system, all patients with flu-like syndrome in different cities of the province should be referred to this center, and nasopharyngeal samples from patients suspected to influenza should be taken and confirmed by PCR.

3.1.2. Study Population

This study was conducted using the files of all patients with confirmed influenza (outpatients vs. inpatients) referred to referral centers in Mashhad from different cities of Khorasan Razavi province.

3.1.3. Sample Collection

A nasopharyngeal swab was obtained for detection of virus by RT-PCR. The samples were placed in transport medium, maintained at 4°C, and sent within 72 h to reference laboratory, where all samples were stored at -70°C. Then, we studied all data related to the confirmed cases, including sex, age, residency, risk factors, history of vaccination, complications, and clinical outcomes.

4. Results:

In this study, a total of 2977 patients (3% outpatients vs. 97% hospitalized) with flu-like syndrome were tested by RT-PCR for influenza during autumn and winter of 2018. Out of 84 outpatients, only two cases were positive for influenza (one patient with Type A and one with type B). Among the hospitalized patients, 80 (51% male vs. 49% female; age range: 1 - 87 years) cases had positive RT-PCR test for influenza. Underlying conditions were identified in nine (10.9%) cases (diabetes: two cases; chronic obstructive pulmonary disease (COPD): one case; chronic cardiac disease: three cases; one pregnant woman; and two patients had a history of seizure). Complications occurred in 18 hospitalizes patients, and pneumonia was the most common complication (17 cases had pneumonia and one case had myocarditis). Death happened in 29 (35.36%) patients and three (33.33%) cases with risk factors. Unfortunately, there was no history of vaccination in our patients. The highest number of patients with influenza (31 [37.8%]) had been reported from district No. 3 of Mashhad municipality, where people have low income and live near the holy shrine, which is a crowded place.

5. Discussion

In this study, 82 cases had confirmed influenza and most of the patients with confirmed influenza were hospitalized people. The results revealed that there was a high rate of disease in certain areas of Mashhad, as well as some cities of Khorasan Razavi province. However, this does not necessarily indicate that these regions are hot spots for influenza virus, because we need suitable indicators to diagnose the clustering of the disease in the mentioned areas. In our study, about 95% of confirmed cases were infected with type A virus, and among the subtyped samples (11 samples), seven cases had virus type A (H3N2) and four patients

had influenza type A (H1N1). In a study by Hosseini conducted between 2011 and 2015, out of 7684 positive cases for influenza, 71% of cases were involved with type A virus and 28% of cases had type B virus. In a recent study in 2015, type A influenza virus was the most common type in comparison with other types of confirmed viruses. However, in 2011, type B virus was the most prevalent type among the other viruses (7). The results of a similar study in Australia revealed that type A (71% of cases) was more prevalent in comparison with other types of influenza viruses (29). Another study in Gorgan, Iran by Javid et al. showed that among 790 suspected cases for influenza, pandemic A H1N1, A/H3N2, and influenza B viruses were confirmed in 3.2%, 2.7%, and 2.8%, respectively. In their survey, the greatest number of confirmed cases with RT-PCR occurred in the age group of 25-34 years (30). In our study, the highest prevalence (39%) occurred in the age range of 40-59 years. Also, most death cases happened in patients aged over 60 years and in those having risk factors. In our patients, the disease led to complications in 29% (18 cases) of patients, and pneumonia was the most prevalent complication (17 cases). One patient died due to myocarditis. In the study conducted in Gorgan, among the confirmed cases, 10.3% were male, and 89.7% were female with a mean age of 29.7 years, and there were 22 people aged > 65 years. Li et al. in 2011 showed that the influenza type A was more common in female patients than males (31). However, in our study, influenza was more common in males than females (51.25% vs. 48.75%). In the study by Javid et al. (30), the peak incidence of disease happened in December; considering the age groups and job type, this peak can be attributed to the transmission of influenza virus and other respiratory viruses in schools and universities. Living in crowded places is a serious risk factor for the transmission of virus. A study by Panning et al. showed that crowded places are a major risk factor for transmission of respiratory viral infections such as influenza (32). Fukusumi et al. conducted a study from 2012 to 2015 among engineers, station staff, and train crew at a railway company. This study defined the attack rates for 2012/13, 2013/14, and 2014/15 seasons as 4.7%, 5.2%, and 7.8%, respectively. Also, they showed that the prevalence rate in railway staff was not more than general population, which could be due to a good ventilation in railway stations in Japan and mass vaccination in the company (33). Bus and taxi drivers, bank staff, bakers, barbers, and health care workers are at a higher risk of getting influenza. People working in the transportation companies like airlines, bus drivers, and postal employees are at a higher risk for getting the illness and about 1.5 times more likely to be admitted to a hospital for seasonal influenza compared to other jobs. Food service staff, people working in accommodation jobs, and educators were among 9-10% of the total number of patients hospitalized due to influenza; also, health care workers accounted for more than 16% of all hospitalizations (34). The study by Jaakkola revealed that secretaries, janitors, and cleaners had the highest rate of getting infected with the virus. Secretaries usually have a higher social contact with people, and they are more at risk for infection. Shared office space has been shown to increase the risk for influenza, common cold, and other respiratory viruses (35). Unfortunately, there was no data about occupation in our registered patients. Pregnant women are susceptible to severe influenza. Physiologic changes related to pregnancy, such as decreased cell-mediated immunity, can increase susceptibility to infection in pregnant women. During the H1N1 pandemic in 2009, severe flu infection among postpartum women (delivered within previous two weeks) was reported (36, 37). In a case series conducted in 2009 during H1N1 pandemic, 20% of deaths were reported among 280 pregnant women admitted to intensive care units (ICUs) (36-39). In the present study, only two pregnant women were reported with influenza, one of whom died due to severe disease and pneumonia. Certain environments such schools, universities, and meetings can accelerate the transmission of the virus. This happens commonly in crowded and contaminated spaces in which the virus is more likely to spread through direct contact. Therefore, shared workplaces and schools can cause flu outbreaks and epidemics, if the employees do not stay home when they are sick and have an active infection. In our survey, the highest number of patients with influenza had been reported from district No. 3 of Mashhad, where the people have low income and live near holy shrine, which is a crowded place. Similarly, Panning et al. reported that crowded places can increase the transmission of flu infection from patients to others (32).

5.1. Conclusions

Our results showed a high prevalence of complication and death among hospitalized patients, especially those without any risk factor for influenza viruses. Therefore, comprehensive vaccination programs and promotion of knowledge about transmission routes are two important factors for disease prevention and lower death rates. Further studies about the risk factors, history of vaccination, job type, and virus type and subtype are recommended in Iran.

5.2. Strengths

The Iranian "National Surveillance System for Influenza" was established in 2004. It is a national system used for sixteen years to collect all data about patients with influenza like illness (ILI) and influenza infection referred

to health centers and hospitals in capital cities of Iranian provinces. The use of such data is a unique approach to provide better information about disease and patients. It is important to teach staff and improve their activities for collecting data and better surveillance.

5.3. Limitations

The main limitations of this study were as follows:

1- Many patients with mild influenza, such as health care workers, may not refer to a laboratory for confirmation of infection.

2- Due to the widespread nature of the flu and since most people do not take treatments, our results cannot reveal a real estimate of the prevalence and clinical outcomes of the disease.

Footnotes

Authors' Contribution: Study concept and design: Ashraf Tavaneee–Sani and Roshanak Sharifi. Acquisition of data and analysis: Zahra Nehbandani, Hassan Masoudi, and Roshanak Sharifi. English language editor: Yasaman Solouki.

Conflict of Interests: The authors declare that there is no conflict of interests.

Data Reproducibility: The data presented in this study is openly available in one of the repositories or will be available on request from the corresponding author by this journal representative at any time during submission or after publication. Otherwise, all consequences of possible withdrawal or future retraction will be with the corresponding author.

Ethical Approval: The study was approved by the Ethics Committee of Mashhad University of Medical Sciences (Project No.1399.692).

Funding/Support: This research was financially supported by the Vice Chancellor for Research of Mashhad University of Medical Sciences.

Informed Consent: All data was taken from the files of patients referred to the Surveillance System for Influenza in Mashhad (Razavi Khorasan, Iran) during autumn and winter 2019. We also used checklists for collecting the data.

References

1. Pretorius MA, Tempia S, Walaza S, Cohen AL, Moyes J, Variava E, et al. The role of influenza, RSV and other common respiratory viruses in severe acute respiratory infections and influenza-like illness in a population with a high HIV sero-prevalence, South Africa 2012-2015. *J Clin Virol*. 2016;**75**:21–6. doi: 10.1016/j.jcv.2015.12.004. [PubMed: 26741826]. [PubMed Central: PMC5712432].
2. Akturk H, Sutcu M, Badur S, Torun SH, Citak A, Erol OB, et al. Evaluation of epidemiological and clinical features of influenza and other respiratory viruses. *Turk Pediatri Ars*. 2015;**50**(4):217–25. doi: 10.5152/TurkPediatriArs.2015.2827. [PubMed: 26884691]. [PubMed Central: PMC4743864].
3. Al Johani SM, Al Balawi M, Al Alwan B, Al Hefdhi R, Hajeer A. Validity of two rapid point of care influenza tests and direct fluorecence assay in comparison of real time PCR for swine of origin Influenza virus. *J Infect Public Health*. 2011;**4**(1):7–11. doi: 10.1016/j.jiph.2010.10.004. [PubMed: 21338954].
4. Howard PF, McCaw JM, Richmond PC, Nissen M, Sloots T, Lambert SB, et al. Virus detection and its association with symptoms during influenza-like illness in a sample of healthy adults enrolled in a randomised controlled vaccine trial. *Influenza Other Respir Viruses*. 2013;**7**(3):330–9. doi: 10.1111/j.1750-2659.2012.00395.x. [PubMed: 22712831]. [PubMed Central: PMC5779839].
5. Jeng K, Massire C, Zembower TR, Deyde VM, Gubareva LV, Hsieh YH, et al. Monitoring seasonal influenza A evolution: Rapid 2009 pandemic H1N1 surveillance with an reverse transcription-polymerase chain reaction/electro-spray ionization mass spectrometry assay. *J Clin Virol*. 2012;**54**(4):332–6. doi: 10.1016/j.jcv.2012.05.002. [PubMed: 22673129]. [PubMed Central: PMC3495324].
6. Fouchier RA, Munster V, Wallensten A, Bestebroer TM, Herfst S, Smith D, et al. Characterization of a novel influenza A virus hemagglutinin subtype (H16) obtained from black-headed gulls. *J Virol*. 2005;**79**(5):2814–22. doi: 10.1128/JVI.79.5.2814-2822.2005. [PubMed: 15709000]. [PubMed Central: PMC548452].
7. Hosseini S, Karami M, Farhadian M, Mohammadi Y. Seasonal activity of influenza in Iran: Application of influenza-like illness data from sentinel sites of healthcare centers during 2010 to 2015. *J Epidemiol Glob Health*. 2018;**8**(1-2):29–33. doi: 10.2991/j.jegh.2018.08.100. [PubMed: 30859784]. [PubMed Central: PMC7325813].
8. Sharify Mood F, Tabatabaei SM, Sharifi-Mood B, Khalili T, Arbabi N, Metanat M, et al. The prevalence of respiratory viruses among patients with influenza-like illness in Zahedan, Southeastern Iran. *Arch Clin Infect Dis*. 2019;**14**(3). doi: 10.5812/archcid.77089.
9. Moghoofei M, Monavari SH, Mostafaei S, Hadifar S, Ghasemi A, Babaei F, et al. Prevalence of influenza A infection in the Middle-East: A systematic review and meta-analysis. *Clin Respir J*. 2018;**12**(5):1787–801. doi: 10.1111/crj.12758. [PubMed: 29316311].
10. Afzali H, Nematian M, Rajabi J, Soleimani Z, Momen-Heravi M, Salehi A, et al. Epidemiological survey of confirmed influenza A (H1N1) in Kashan, Aran and Bidgol cities during 2009-10. *KAUMS J (FEYZ)*. 2011;**15**(3):259–66.
11. Milosevic I, Korac M, Popovic N, Lavadinovic L, Urosevic A, Milosevic B, et al. Influenza A H1N1 virus infection among pregnant women in a tertiary hospital in Belgrade, Serbia. *J Infect Dev Ctries*. 2018;**12**(5):380–4. doi: 10.3855/jidc.8454. [PubMed: 31865302].
12. Yavarian J, Shafiei Jandaghi NZ, Naseri M, Hemmati P, Dadras M, Gouya MM, et al. Influenza virus but not MERS coronavirus circulation in Iran, 2013-2016: Comparison between pilgrims and general population. *Travel Med Infect Dis*. 2018;**21**:51–5. doi: 10.1016/j.tmaid.2017.10.007. [PubMed: 29031546]. [PubMed Central: PMC7110681].
13. Ortiz JR, Neuzil KM, Shay DK, Rue TC, Neradilek MB, Zhou H, et al. The burden of influenza-associated critical illness hospitalizations. *Crit Care Med*. 2014;**42**(11):2325–32. doi: 10.1097/CCM.0000000000000545. [PubMed: 25148596]. [PubMed Central: PMC4620028].
14. Tavakoli A, Karbalaie Niya MH, Bokharaei-Salim F, Farahmand M, Izadi M, Dorostkar R, et al. The molecular epidemiology of respiratory viruses in military trainees in Iran. *Med J The Islamic Republic of Iran (MJIRI)*. 2019. doi: 10.47176/mjiri.33.40.
15. Centers for Disease Control and Prevention. Estimated influenza illnesses, medical visits, and hospitalizations averted by vaccination in the United States. *CDC*. 2018.

16. Sullivan SG, Tay EL, Kelly H. Variable definitions of the influenza season and their impact on vaccine effectiveness estimates. *Vaccine*. 2013;**31**(40):4280–3. doi: 10.1016/j.vaccine.2013.06.103. [PubMed: 23850417].
17. Moasser E, Behzadian F, Moattari A, Fotouhi F, Rahimi A, Zaraket H, et al. Molecular characterization and phylogenetic analysis of human influenza A viruses isolated in Iran during the 2014-2015 season. *Arch Virol*. 2017;**162**(7):1975–84. doi: 10.1007/s00705-017-3323-3. [PubMed: 28331993].
18. Almeida A, Codeco C, Luz PM. Seasonal dynamics of influenza in Brazil: The latitude effect. *BMC Infect Dis*. 2018;**18**(1):695. doi: 10.1186/s12879-018-3484-z. [PubMed: 30587159]. [PubMed Central: PMC6307116].
19. Zhand S, Tabaraei A, moradi A, Fotoohi F, Javid N, Bazoori M, et al. Detection of seasonal influenza H1N1 and H3N2 viruses using RT-PCR assay during 2009 flu pandemic in Golestan Province. *Med Lab J*. 2014;**8**(2):27–32.
20. Khondabi M, Karami M, Roshanaei G, Azizi Jalilian F, Shojaeian M, Bathaei SJ, et al. An epidemiological study on Influenza-like syndrome: Descriping reported cases to the Influenza surveillance system in Hamadan province during 2013 and 2014. *Razi J Med Sci*. 2017;**23**(151).
21. Alborzi A, Aelami MH, Ziyaeyan M, Jamalidoust M, Moeini M, Pourabbas B, et al. Viral etiology of acute respiratory infections among Iranian Hajj pilgrims, 2006. *J Travel Med*. 2009;**16**(4):239–42. doi: 10.1111/j.1708-8305.2009.00301.x. [PubMed: 19674262].
22. Loubet P, Lenzi N, Valette M, Foulongne V, Krivine A, Houhou N, et al. Clinical characteristics and outcome of respiratory syncytial virus infection among adults hospitalized with influenza-like illness in France. *Clin Microbiol Infect*. 2017;**23**(4):253–9. doi: 10.1016/j.cmi.2016.11.014. [PubMed: 27903461]. [PubMed Central: PMC7128342].
23. Piralla A, Mariani B, Rovida F, Baldanti F. Frequency of respiratory viruses among patients admitted to 26 Intensive Care Units in seven consecutive winter-spring seasons (2009-2016) in Northern Italy. *J Clin Virol*. 2017;**92**:48–51. doi: 10.1016/j.jcv.2017.05.004. [PubMed: 28527970]. [PubMed Central: PMC7172430].
24. Javid Khojasteh V, Mojtahedi A, Hosseini S, Joukar F. Relative frequency of influenza A/H1N1 virus in Guilan province, Iran. *Iran J Med Microbiol*. 2017;**11**(5):83–9.
25. Chemaly RF, Vigil KJ, Saad M, Vilar-Compte D, Cornejo-Juarez P, Perez-Jimenez C, et al. A multicenter study of pandemic influenza A (H1N1) infection in patients with solid tumors in 3 countries: early therapy improves outcomes. *Cancer*. 2012;**118**(18):4627–33. doi: 10.1002/cncr.27447. [PubMed: 22359314].
26. Dowdle WR, Millar JD, Schonberger LB, Ennis FA, LaMontagne JR. Influenza immunization policies and practices in Japan. *J Infect Dis*. 1980;**141**(2):258–64. doi: 10.1093/infdis/141.2.258. [PubMed: 7365278].
27. Esghaei M, Moghoofei M, Keshavarz M, Keyvani H, Bokharaei-Salim F, Farahmand M, et al. Trends in surveillance data of influenza virus in Tehran before decreasing dispatch of Iranian Hajj pilgrims to Mecca. *Med J Islam Repub Iran*. 2018;**32**:41. doi: 10.14196/mjiri.32.41. [PubMed: 30159292]. [PubMed Central: PMC6108279].
28. Adam DC, Scotch M, MacIntyre CR. Phylodynamics of Influenza A/H1N1pdm09 in India Reveals Circulation Patterns and Increased Selection for Clade 6b Residues and Other High Mortality Mutants. *Viruses*. 2019;**11**(9). doi: 10.3390/v11090791. [PubMed: 31462006]. [PubMed Central: PMC6783925].
29. O'Brien K, Barr IG. Annual report of the National Influenza Surveillance Scheme, 2006. *Commun Dis Intell Q Rep*. 2007;**31**(2):167–79. [PubMed: 17724991].
30. Javid N, Moradi A, Tabarraei A, Bazouri M. Clinical and epidemiological profile of pandemic influenza A H1N1, H3N2, and Type B in the Southeast of Caspian Sea, Iran. *Jundishapur J Microbiol*. 2017;**10**(3). doi: 10.5812/jjm.35616.
31. Li T, Liu Y, Di B, Wang M, Shen J, Zhang Y. Epidemiological investigation of an outbreak of pandemic influenza A (H1N1) 2009 in a boarding school: serological analysis of 1570 cases. *J Clin Virol*. 2011;**50**(3):235–9. doi: 10.1016/j.jcv.2010.11.012. [PubMed: 21195022].
32. Panning M, Eickmann M, Landt O, Monazahian M, Olschlager S, Baumgarte S, et al. Detection of influenza A(H1N1)v virus by real-time RT-PCR. *Euro Surveill*. 2009;**14**(36). [PubMed: 19758541].
33. Fukusumi M, Kanagawa Y, Ohfuji S, Miyazaki K, Matsui T, Mizoguchi K, et al. Risk of seasonal influenza by occupation in a railway company in a metropolitan area of Japan during three influenza seasons. *Jpn J Infect Dis*. 2020;**73**(4):268–71. doi: 10.7883/yoken.JJID.2019.245. [PubMed: 32115539].
34. SHRM Executive Network. *Some jobs pose more risk for contracting flu*. 2014. Available from: https://www.shrm.org/resourcesandtools/hr-topics/risk-management/pages/jobs-risk-contracting-flu.aspx.
35. Jaakkola JJ, Heinonen OP. Shared office space and the risk of the common cold. *Eur J Epidemiol*. 1995;**11**(2):213–6. doi: 10.1007/BF01719490. [PubMed: 7672078].
36. Louie JK, Acosta M, Jamieson DJ, Honein MA, California Pandemic Working G. Severe 2009 H1N1 influenza in pregnant and postpartum women in California. *N Engl J Med*. 2010;**362**(1):27–35. doi: 10.1056/NEJMoa0910444. [PubMed: 20032319].
37. Mosby LG, Rasmussen SA, Jamieson DJ. 2009 pandemic influenza A (H1N1) in pregnancy: a systematic review of the literature. *Am J Obstet Gynecol*. 2011;**205**(1):10–8. doi: 10.1016/j.ajog.2010.12.033. [PubMed: 21345415].
38. Kourtis AP, Read JS, Jamieson DJ. Pregnancy and infection. *N Engl J Med*. 2014;**370**(23):2211–8. doi: 10.1056/NEJMra1213566. [PubMed: 24897084]. [PubMed Central: PMC4459512].
39. Siston AM, Rasmussen SA, Honein MA, Fry AM, Seib K, Callaghan WM, et al. Pandemic 2009 influenza A(H1N1) virus illness among pregnant women in the United States. *JAMA*. 2010;**303**(15):1517–25. doi: 10.1001/jama.2010.479. [PubMed: 20407061]. [PubMed Central: PMC5823273].