

## Original Research

### Clinical And Preclinical Finding In Influenza

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#### Abstract:

**Background:** Influenza is an acute respiratory viral infection that threatens global health. Regular assessment of clinical and paraclinical symptoms is a very important tool for early diagnosis and disease management, transmission, and prevention of influenza, epidemics. The main purpose of this study was to evaluate the clinical and paraclinical symptoms of patients with influenza in the north of Iran.

**Methods:** This descriptive cross-sectional study was conducted on hospitalized patients through a convenience sampling method from September 2019 to February 2020 in a teaching hospital, in Iran. The inclusion criteria were age at least one year and the possibility of influenza based on at least one of the following clinical and paraclinical findings. Clinical manifestation, radiographic findings, and paraclinical findings had been assessed. Patients with hospitalization of fewer than three days and incomplete documents were excluded.

**Results:** Most of the patients were male (52.0%) and had a history of contact with positive influenza patients (88.3%). The most common symptoms were fever (89.9%), chills (76.9%), cough (67.5%), and sore throat (41.2%), respectively. It was no significant difference between WBC, LDH, and CPK in less than 12 years old vs. above 12 years old ( $p>0.05$ ). But, the platelet was a significant difference between less than 12 years old vs. above 12 years old.

**Conclusions:** The results of the present study provide a rationale for annual vaccination and other preventive measures against influenza. Also, this study was the last study in relation to influenza before the COVID-19 pandemic and the extracted data can be useful to compare influenza and COVID-19.

**Keywords:** Influenza Disease, Acute Respiratory Infection, Symptom of Disease

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## Introduction

Influenza is an acute respiratory viral infection that threatens global health and is one of the leading causes of death all over the world (1). Influenza viruses belong to the orthomyxoviridae family. The virus is divided into three types A, B, C based on the difference between nucleoprotein and protein matrix antigens, and type A divided to 16 serotype and 8 serotypes based on hemagglutinin component and Neuroaminidase, respectively (2). The virus causes disease in mammals, birds and humans. The incubation period is one to four days, and the transmission period is from the first day to 5-7 days after the onset of symptoms. Symptoms include a sudden onset of fever, cough, sputum, headache, joint and muscle pain, severe weakness, sore throat, and rhinorrhea (3). Gastrointestinal symptoms, including nausea, vomiting, and diarrhea, are also common (4). Clinical symptoms play an important role in the rapid diagnosis and management of the disease. Complicated influenza and also children under six months have higher mortality rate (5, 6). Primary treatment is supportive approach. Antiviral treatment is recommended in the following patients: patient at least 65 years old, people with underlying disease including chronic heart disease, respiratory, renal, liver, neurological and metabolic disease, patient undergone immunosuppressive medications such as chemotherapy, long term steroid therapy, pregnant women up to two weeks after delivery and people with Body Mass Index (BMI) at least 40 (7, 8).

The main strategy for prevention of the flu is seasonal vaccination (9). The virus finds small genomic changes (drift) each winter resulting epidemics. It also has extensive genomic changes (shift) over long period time, creating a global pandemic (10, 11). Regular assessment of clinical and paraclinical symptoms is a very important tool for early diagnosis and disease management, transmission and prevention of

influenza, epidemics and pandemics. Otherwise, the highly contagious virus will spread rapidly in a short period of time (2,12, 13). So, the main purpose of this study was to evaluate the clinical and paraclinical symptoms of patients with influenza in Mazandaran province, north of Iran.

## Material and Methods

This descriptive cross-sectional study was conducted on hospitalized patients through convenience sampling method from September 2019 to February 2020 in teaching and referral hospital of Qaemshahr city, Mazandaran province, Iran. The above hospital is a center of infectious disease and admitted the most patients with influenza diagnosis. The inclusion criteria were age at least one year and possibility of influenza based on at least one of the following clinical and paraclinical finding. Clinical manifestation included fever, coughing, respiratory distress, dyspnea, crackles, vomiting, cyanosis, diarrhea and infectious coryza. Radiographic finding included pulmonary infiltration, collapsed lung and pleural effusion. Paraclinical finding included WBC < 10000 or > 15000, ESR  $\geq$  30, elevated CRP (qualitative) and positive RT-PCR test. Patients with hospitalization less than three days and incomplete documents were excluded. This study was registered and approved by the ethics committee of the Mazandaran University of Medical Science (code: IR. MAZUMS. REC.1399.8108). All included participants signed written informed consent.

The questionnaire consisted of two parts. Demographic part included age, gender, marital status, hospitalization day, history of contact with influenza patient and so on. Clinical and paraclinical parts assessed clinical manifestation, radiographic and paraclinical finding of influenza disease. Then descriptive statistics including mean, standard deviation and frequency had been used. Also, t-test and

chi-square tests were used to compare the variables. The SPSS version 18 was used to analyze the data. Also, p-value less than 0.05 considered statistically significant.

## Results

The demographic characteristics of influenza are shown in table1. Most of the patients were male (52.0%) and had the history of contact with positive influenza patient (88.3%). The mean (SD) of age and hospitalization days were 35.9 (24.0) and 4.6(2.8) days, respectively.

The clinical manifestations of influenza disease are shown in table2. The most common symptoms were fever (89.9%), chills (76.9%), cough (67.5%) and sore throat (41.2%), respectively.

According to the table 3, paraclinical finding of influenza disease stratified by age is shown. The results showed it was not significant difference between WBC, LDH and CPK in less than 12 years old vs. above 12 years old ( $p>0.05$ ). But, the platelet was significant different between less than 12 years old vs. above 12 years old ( $p=0.001$ ).

The radiographic finding showed most of the influenza patients had multi lobar involvement in chest X-ray (50.4%) but unilateral involvement in lung CT-scan (54.7%). Also, significant difference was seen between less than 12 years old vs. above 12 years old in term of lung involvement ( $p=0.038$ ) (table5).

## Discussion

According to the results of present study, most of the patients were male and had history of contact with positive influenza patients. Also, significant difference was seen between less than 12 years old vs. above 12 years old in term of platelet and lung involvement.

The average age of the patients was 35 years old. Lia study showed patients aged 40 to 51 years old had higher risk of infection (14). Also, another study in northern Iran showed

influenza infection was more prevalent in age group 21 to 30 years old (15). Lower rate of influenza among older adults and children may be due to annually vaccination in elderlies and higher antibodies in children secondary to childhood viral infection.

In the present study, the influenza infection was more prevalent in male patients. Javadian study showed the prevalence of influenza was higher in female 64.2% (16). But in another study in Kashan the rate of infection was not significant between male and female (44 vs. 43 patients) (17). Yan study showed the prevalence of influenza was higher in male 62.4%(18). In spite of this prevalence, both males and females are susceptible to influenza and personal protection should be done.

The results of the present study showed most of the patients had history of contact with positive influenza patient. Lia study showed contact to suspected influenza patients may increase two times the chance of influenza infection (14). These results showed quarantine and maintain social distance are the main preventive strategy to protect itself from influenza infection.

The mean of hospitalization was 4.6 days. Similar to the current study, in Kashan the mean hospitalization day was 4 days (17).()

In the present study, the most common symptoms were fever, chills, cough and sore throat, respectively. But in Javadian study the most common complaints were respiratory symptoms, fever and myalgia, respectively (16). In Kashan study the most clinical manifestation was fever and cough (17). Nypaver study showed fever and myalgia are the most common manifestation(19). Yan study showed fever and cough are the most common symptoms(18).

The limitation of the present study was loss to follow up of the patients. The results of the present study provide rational for annual vaccination and other prevention measurement against influenza. Also, this study was the last study in relation to the influenza before

COVID-19 pandemic and the extracted data can be useful to compare the influenza and COVID-19. On the other hand, influenza characteristics could predict COVID-19 pandemic.

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**Conflict of Interest:** None.

### References

1. Mohebbi A FF, Jamali A, Yaghobi R, Farahmand B, Mohebbi R. . Molecular epidemiology of the hemagglutinin gene of prevalent influenza virus A/H1N1/pdm09 among patient in Iran. *Virus research*. 2019;259:38-45.
2. Ryu S, Cowling BJ. Human influenza epidemiology. *Cold Spring Harbor Perspectives in Medicine*. 2021;11(12):a038356.
3. Wang Y ST, Li K, Jin Y, Yue J, Ren H, et al. . Different subtypes of influenza viruses target different human proteins and pathways leading to different pathogenic phenotypes. . *BioMed research international*. 2019:2019.
4. Sanz J, MT VA. Influenza and cardiorespiratory events: a clinical-epidemiological review with a multidisciplinary point of view. *Revista Espanola de Quimioterapia: Publicacion Oficial de la Sociedad Espanola de Quimioterapia*. 2021;34(6):556-68.
5. Yokomichi H MM, Lee JJ, Kojima R, Yokoyama T, Yamagata Z. Incidence of hospitalisation for severe complications of influenza virus infection in Japanese patients between 2012 and 2016: a cross-sectional study using routinely collected administrative data. . *BMJ open*. 2019;9(1):e024687.
6. Maldonado YA, O'Leary ST, Ardura MI, Banerjee R, Bryant KA, Campbell JD, et al. Recommendations for prevention and control of influenza in children, 2021–2022. *Pediatrics*. 2021;148(4).
7. Stewart RJ FB, Chung JR, Gaglani M, Reis M, Zimmerman RK, et al. Influenza antiviral prescribing for outpatients with an acute respiratory illness and at high risk for influenza-associated complications during 5 influenza seasons—United States, 2011–2016 . *Clinical Infectious Diseases*. 2018;66(7):1035-41.
8. Lee K, Chen Y-H, Huang C-H, Hsu J-C, Chang Y-C, Kuo H-J, et al. A multicenter cohort study of severe dengue and critically ill influenza patients with elevated cardiac troponin-I: Difference clinical features and high mortality. *Travel Medicine and Infectious Disease*. 2022;47:102281.
9. Campos-Outcalt D. Influenza vaccine update, 2021–22. *The Journal of Family Practice*. 2021;70(8):399-402.
10. Ward BJ MA, Séguin A, Pillet S, Trépanier S, Dhaliwall J, et al. . Efficacy, immunogenicity, and safety of a plant-derived, quadrivalent, virus-like particle influenza vaccine in adults (18–64 years) and older adults (≥ 65 years): two multicentre, randomised phase 3 trials. . *The Lancet*. 2020.
11. Palomba E, Castelli V, Renisi G, Bandera A, Lombardi A, Gori A, editors. *Antiviral Treatments for Influenza. Seminars in Respiratory and Critical Care Medicine*; 2021: Thieme Medical Publishers, Inc.
12. Tchilian E HB, Morgan SB, Martini V, Sharma R, Clark B, et al. Immunogenicity and protective efficacy of seasonal human

- live attenuated cold-adapted influenza virus vaccine in pigs. *Frontiers in immunology*. 2019;10:2625.
- 13.Kharroubi G, Cherif I, Bouabid L, Gharbi A, Boukthir A, Ben Alaya N, et al. Influenza vaccination knowledge, attitudes, and practices among Tunisian elderly with chronic diseases. *BMC geriatrics*. 2021;21(1):1-9.
- 14.Liu Y, Wang Y, Mai H, Chen Y, Liu B, Liu Y, et al. Clinical characteristics, risk factors and antiviral treatments of influenza in immunosuppressed inpatients in Beijing during the 2015–2020 influenza seasons. *Virology Journal*. 2022;19(1):1-11.
- 15.Haghsheenas M, Jafarian E, Babamahmoodi F, Tabrizi A, Nandoost S, Alizadeh-Navaei R. Prevalence of influenza A/H3N2 virus in northern Iran from 2011 to 2013. *Caspian journal of internal medicine*. 2015;6(2):116.
- 16.Javanian M, Babazadeh A, Ebrahimpour S, Shokri M, Bayani M. Clinical and laboratory findings of patients with the possible diagnosis of influenza hospitalized in affiliated hospitals of Babol University of Medical Sciences, 2015-2016. *Current Issues in Pharmacy and Medical Sciences*. 2018;31(3):113-6.
- 17.Momen-Heravi M, Afzali H, Soleimani Z, Sharif A, Razzaghi R, Moravvegi SA, et al. Clinical Presentation and Final Outcome in Definite Cases of Influenza A (H1N1) in Kashan, Iran. *Zahedan J Res Med Sci*. 2015;17(1):37-9.
- 18.Yan Q, Zhong J, Zhou H, Zhou J. Clinical and epidemiological characteristics of 245 cases of influenza A (H3N2). *Zhonghua jie he he hu xi za zhi= Zhonghua Jiehe he Huxi Zazhi= Chinese Journal of Tuberculosis and Respiratory Diseases*. 2019;42(7):510-4.
- 19.Nypaver C, Dehlinger C, Carter C. Influenza and influenza vaccine: A review. *Journal of Midwifery & Women's Health*. 2021;66(1):45-53.

## Tables

**Table1: The demographic characteristics of influenza patients (N=308)**

Variables		Frequency (%)
Gender	Female	148 (48.0)
	Male	160 (52.0)
History of contact with positive influenza patient	Yes	272 (88.3)
	No	36 (11.7)
Mean (SD)		
Age (Year)		35.9 (24.0)
Hospitalization days		4.6 (2.8)

**Table2. Clinical manifestation of influenza disease**

Variable	Frequency (%)
Fever	277 (89.9%)
Chills	237 (76.9%)
Cough	208 (67.5%)
Sore throat	127 (41.2%)

**Table3. Paraclinical finding of influenza disease stratified by age**

Variable	Age ≤ 12 years	Age > 12 years	Statistical test and <i>p</i> -value
WBC	7543.42 (4111)	7856.11 (5789.45)	<i>p</i> = 0.817 *
Plt	218850 (73724.16)	196615.28 (114155.74)	<i>p</i> = 0.001 *
LDH	585.0 (208.8)	496.6 (241.2)	<i>p</i> = 0.475 *
CPK	424.28 (213.0)	612.51 (383.8)	<i>p</i> = 0.215 *

**Table4. Radiographic finding of influenza disease**

Variable		Frequency (%)
Chest X-ray (N=127)	Unilateral	63 (49.6)
	Multi-lobar	64 (50.4)
Lung CT-scan (N=106)	Unilateral	58 (54.7)
	Multi-lobar	48 (45.3)

**Table5. Radiographic finding of influenza disease stratified by age**

Age group Lung involvement	>12-years-old	< 12-years-old	P-value
Yes	52 (59.8%)	16 (40.0%)	0.038