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Epidemiology of Influenza in Fars Province, Southern Iran; a Population-Based Study (2015–2019)

Hossein Faramarzi, MD[1]; Razieh Sadat Mousavi-Roknabadi, MD[2*]; Abdolrasoul Hemmati, Phram D[3]; Ali Faramarzi[4]; Hamid Bakhtiari, MD[5]

[1]Department of Community Medicine, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
[2]Department of Emergency Medicine, Faculty of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
[3]Vice-Chancellor of Health Affairs, Non-Communicable Diseases Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
[4]Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran
[5]Department of Communicable Disease Control, Vice Chancellor of Health, Shiraz University of Medical Sciences, Shiraz, Iran

Abstract

Background: Influenza is one of the most important viral diseases with high mortality and morbidity that can have a great impact on public health and economy.
Objective: To investigate the clinical and epidemiological features of influenza virus A/H1N1, A/H3N2, and B infection in Fars province, southern Iran, in 2015-2019.
Methods: In this retrospective cross-sectional study, we assessed the archived data of Syndromic Surveillance System of Iran's Health Ministry, allowed access by Communicable Diseases' Unit of Health chancellor of Shiraz University of Medical Sciences, from December 22, 2015 to September 22, 2019. The participants included all patients whose data were recorded as influenza-like illness (ILI) and severe acute respiratory infections/illness (SARI). Influenza viral infection was confirmed by reverse-transcriptase polymerase chain reaction (RT-PCR).
Results: Totally, 1269 patients suspected of influenza were sampled. The mean ± SD of age was 29.40 ± 26.91 years. Fever was the most common symptom (68.6%). The highest incidence was in winter (55.9%). Of 928/1269 laboratory's results which were recorded in the registry, 204 (16.08%) samples were positive and 724 (57.05%) were negative. Among 204 positive results, 191 (15.05%) were influenza type A, and 8 (0.63%) influenza type B. Among patients with definite influenza type A, 34 (2.68%) had H1N1/p subtype, 58 (4.57%) H3N2, and one (0.08%) had other subtypes; however, subtypes were not identified in 7.72% of patients. Six (3.0%) patients with confirmed influenza expired.
Conclusion: The incidence of influenza, especially type A, in Fars province, southern Iran is considerable and requires more attention for prevention in health policy programs.
Keywords: Influenza, Influenza A, Influenza A/H3N2, Influenza A/H1N1, Influenza B
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Introduction

Influenza is one of contagious viral diseases caused by an RNA virus from the *Orthomyxoviridae* family.[1] Through pandemics, epidemics, outbreaks, and sporadic cases, influenza causes high mortality, puts more people at risk of serious complications, and causes immunity in a huge number of individuals.[2] Three types of influenza are known in which two types of superficial glycoproteins, NA and HA, exist in types A and B, while influenza C has only one glycoprotein on its surface. Totally, 16 types of H and 9 types of N antigens are identified of which A/H1N1 is the most common.[3] The epidemiological patterns of these three types of influenza differ markedly. Influenza C virus does not cause epidemics, but makes mild respiratory infections sporadically. Influenza B virus sometimes causes epidemics, and pandemics are mostly caused by type A. Types B and A/H1N1 were the most prevalent viruses worldwide in recent years, and H3N2 is on the rise.[4-6] Diagnosis is usually based on epidemiological

characteristics. It should be noted that the economic impact of influenza outbreaks is of great importance.[6] The influenza virus infection has different clinical features, and it may not be distinguished from other respiratory viral diseases. So, it is not detectable based solely on symptoms.[7] Correct diagnosis and rapid and appropriate management are important for controlling this disease, which would not be possible without practical laboratory tests.[8] Various tests are available for rapid antigen detection, but confirmation of the influenza viral infection by reverse-transcriptase polymerase chain reaction (RT-PCR)[6] is rapid, cost-effective, sensitive and specific.[8-10] All positive cases should be considered as influenza, and specific treatment should be started as soon as possible. This is crucial in controlling epidemics.[11]

Objective

Because of the importance of this disease, and the need for information about its epidemiology for public health

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Corresponding Author: Razieh Sadat Mousavi-Roknabadi, MD; Emergency Medicine Department, Faculty of Medicine, Shiraz University of Medical Sciences, Namazi Hospital, Postal Code: 71937-11351, Shiraz, IR Iran. Tel: +989131563018, Email: mousavi_razieh@sums.ac.ir

action planning to prevent and control the disease, the aim of the current study was to investigate the clinical and epidemiological features of the influenza virus A/H1N1, A/H3N2, and B infection in Fars province, southern Iran from 2015 to 2019.

Materials and Methods

In this retrospective cross-sectional study, we assessed the archived data of Syndromic Surveillance System of Iran's health ministry, allowed access by Communicable Diseases' Unit of Health chancellor of Shiraz University of Medical Sciences.

The participants included all patients who were referred to one of the health centers in Fars province and their data were recorded as influenza-like illness (ILI) and severe acute respiratory infections/illness (SARI) from December 22, 2015 to September 22, 2019.

ILI is defined as incidence of fever and cough symptoms during the recent week. SARI is defined as fever and cough during the recent week, and hospitalization due to one of the symptoms interfering with the functioning of one of three vital body systems including: 1. respiratory system (tachypnea, or intercostal muscle depression during breathing, or breathing with sound, or bloody sputum), or 2. cardiovascular system (chest pain, or severe hypotension, or rhythmic disorder), or 3. nervous system (decreased consciousness, or seizures). A suspected case of influenza was defined as: fever above 38°C, or having at least two respiratory symptoms (including rhinorrhea, sore throat or cough) plus at least one of the following conditions: history of travel to an epidemic area during the last 7 days, or history of contact with an infected patient, or severe pulmonary disease or any unknown pulmonary disease causing death. Influenza viral infection is confirmed by RT-PCR.[8]

Two types of data were collected: (*a*) demographic information (age, gender, the place of residence, the season and month of the disease) and (*b*) clinical and laboratory findings (symptoms, past medical history, type of viruses, comorbidities, and the patients' status). We checked for data duplication, as well as the validity of data, or if there is strange data or not. For example, before conducting the statistical analysis, the variable of age was recorded as the year of birth in some patients, so we converted it to age. Uncomplete data were considered in the statistical analysis and were recorded as not determined.

All analyses were performed using the SPSS software version 22.0 for Windows, using chi-square and Fisher's exact tests for proportions, and independent *t* and one-way ANOVA tests for the means. The results were presented as mean ± standard deviation (SD) for continuous variables and were summarized in number (percentage) for categorical variables. Two-sided $P < 0.05$ and 95% confidence interval (CI) were considered to be statistically significant. Microsoft Office Excel version 2013 for Windows was used to create diagrams.

Results

During the study period, 1 149 124 patients were referred to 77 Fars province health centers, southern Iran, due to respiratory symptoms, and their data were recorded in the registry system. All 6966 (61%) were suspected of ILI [3,287 (47.2%) males vs. 3,679 (52.8%) females]. Both genders were similar in terms of ILI and SARI ($P = 0.425$). The mean ± SD of age was 32.69 ± 26.44 (range: 0–96) (31.9 ± 27.09 in males and 34.20 ± 25.75 in females, $P = 0.103$, 95% CI = -6.85, 0.63). Samples were taken from 387 patients with ILI, including 289 (74.87%) throat swabs and 20 (5.17%) nasal swabs. The results showed that 60 (15.50%) patients had influenza type A and two (0.52%) had influenza type B. Influenza type A subtype identification was done in 31 patients, of whom nine (2.33%) had H1N1/p and 22 (5.68%) H3N2.

As shown in Table 1, 1735 of the referred patients [841 (48.5%) males and 894 (51.5%) females, $P = 0.794$] were suspected of SARI. The mean ± SD of age was 31.28 ± 27.99 (range: 0–96) years (29.61 ± 28.19 in males and 32.85 ± 27.73 in females, $P = 0.016$, 95%CI = -5.87, -0.61). Samples were taken from 882 patients with SARI, including 668 (75.74%) throat swabs, 151 (17.12%) endotracheal suctions, and 46 (5.21%) nasal swabs, of which 138 (15.65) were positive and 550 (62.38%) were negative. Totally, 131 (14.85%) patients had influenza type A, and six (0.68%) had influenza type B. Among patients with definite influenza type A, 25 (2.83%) had the H1N1/p subtype, 36 (4.08%) the H3N2 subtype, and one (0.11%) had other subtypes, but the subtypes were not identified in other patients.

In both ILI and SARI, the highest incidence was in winter, and the lowest in summer. As shown in Figures 1 and 2, the highest incidence pertained to January-February. In ILI, the disease was on a downward trend from February-March to June-July, followed by an upward trend that peaked in August-September, and then decreased. In the case of SARI, a small peak was seen in April-May.

In general, 1,269 patients suspected of influenza were sampled, including 957 (75.41%) throat swabs, 151 (12.0%) endotracheal suctions, and 66 (5.2%) nasal swabs. The type of sampling was not recorded in other patients. The mean ± SD of age was 29.40 ± 26.91 (range: 0–96) years [28.31 ± 26.89 in males and 30.41 ± 26.90 in females, $P = 0.94$, 95% CI = 1.511, -5.061]. Both genders were sampled equally ($P = 0.73$). The highest incidence was observed in the age group of 0–1 years (23.6%), and the lowest in the age group of 15–24 years (6.0%) (Table 2).

In these patients, fever was the most common symptom (68.6%), and the most common comorbidity was chronic heart disease (14.1%) followed by diabetes (7.6%).

Table 1. Patients' Characteristics With Influenza-Like Illness (ILI) or Severe Acute Respiratory Infections/Illness (SARI) in Southern Iran (2015–2019)

Variables	Patients Suspected of ILI (n = 6966)	Patients Suspected of SARI (n = 1735)
Age (mean ± SD)	32.69 ± 26.44	31.28 ± 27.99
Male	31.9 ± 27.09	29.61 ± 28.19
Female	34.20 ± 25.75	32.85 ± 27.73
P value	0.103 (95% CI = -6.85, 0.63)	0.016* (95% CI = -5.87, -0.61)
Age groups (%)		
0–1	525 (7.53)	413 (23.8)
2–4	569 (8.17)	99 (5.7)
5–14	966 (13.86)	162 (9.3)
15–24	769 (11.05)	118 (6.8)
25–34	1128 (16.20)	193 (11.1)
35–44	872 (12.53)	173 (10.0)
45–54	682 (9.78)	126 (7.3)
55–64	569 (8.17)	170 (9.8)
>65	886 (12.71)	281 (16.2)
Gender (%)		
Male	3287 (47.2)	841 (48.5)
Female	3679 (52.8)	894 (51.5)
P value	0.425	0.794
Season of disease (%)		
Spring	1245 (17.9)	295 (17.0)
Summer	1500 (21.5)	80 (4.6)
Autumn	1429 (20.5)	355 (20.5)
Winter	2792 (40.1)	1005 (57.9)
Laboratory sample (%)		
Total sample	387	882
Throat swab	289 (74.87)	668 (75.74)
Nasal swab	20 (5.17)	46 (5.21)
Endotracheal suction	0 (0)	151 (17.12)
Not determined	78 (20.16)	17 (1.93)
Laboratory result (%)		
Positive	66 (17.05)	138 (15.65)
Negative	174 (44.96)	550 (62.38)
Not determined	147 (37.98)	194 (22.0)
Virus type (%)		
A	60 (15.50)	131 (14.85)
A (H1N1/p)	9 (2.33)	25 (2.83)
A (H3N2)	22 (5.68)	36 (4.08)
Other types	0 (0)	1 (0.11)
Not determined	29 (7.49)	69 (7.82)
B	2 (0.52)	6 (0.68)
Not determined	4 (1.03)	1 (0.11)
Patients' outcome (%)		
Outpatients	6533 (93.8)	0 (0)
Inpatients	433 (6.2)	1693 (97.6)
Death	0 (0)	42 (2.4)

* Statistically significant.

Seventy (5.5%) patients had a history of international travel; Iraq (3.9%) and Saudi Arabia (0.9%) were the most common. Besides, 43 patients (3.39%) reported a history of domestic travel to other cities in Iran a week prior to the onset of symptoms. Also, 38 (2.99%) patients reported a history of contact with birds. Pneumonia (29.7%) was the most common complication.

Also, the highest incidence of influenza was in winter. The influenza had an upward trend that peaked in December-January and January-February, and then decreased. The number of patients had a small increase in August-September (Figure 3).

Of the 928 laboratory results which were recorded in the registry system, 204 (16.08%) samples were positive and 724 (57.05%) were negative. Among the positive results, 191 (15.05%) were influenza type A, and 8 (0.63%) were influenza type B. In five patients, the virus type was not determined. Among patients with definite influenza type A, 34 (2.68%) had the H1N1/p subtype, 58 (4.57%) the H3N2, and one (0.08%) had the other subtypes; subtypes were not identified in 98 (7.72%) patients.

As shown in Table 3, there was no statistically significant difference between the patients with confirmed influenza type A and B in terms of age, gender, history of travel, contact with birds, comorbidities, complications, or outcome. The mortality rate was similar in patients with influenza A and B (P = 0.578). It was found that all patients with confirmed virus type A had complications of primary and secondary pneumonia, cardiopulmonary, acute respiratory distress syndrome (ARDS), as well as bronchitis, and the most common complication was pneumonia. But only one patient (12.5%) with confirmed virus type B had pneumonia, and other complications were not seen.

According to Table 4, there was an association between complications and gender (P = 0.011), and cardiopulmonary was mostly observed in male patients (P = 0.002) with unconfirmed influenza. Pneumonia and bronchitis were mostly found in the age group 0-1 years (P < 0.0001). There was no significant relationship between the complications and other factors. The most commonly prescribed drugs were ceftriaxone (28.6%) and vancomycin (35%). There was no significant statistical association between complications and gender, age groups, history of international and domestic travel, as well as history of contact with birds in patients with confirmed influenza virus type A and B (Supplementary file 1, Table S1).

Totally, 6 (3.0%) patients with confirmed influenza died, and the age group of 35–44 years had the highest rate of mortality (66.7%). There was a significant association between patients' outcome and age group (P = 0.036) (Table 5).

Discussion

In the current study, we investigated the clinical and epidemiological features of influenza virus A/H1N1, A/H3N2, and B infection among patients in Fars province, southern Iran, 2015–2019. The results showed that suspected influenza was more prevalent in the age group of 0–1 (23.6%) and >65 years (13.8%), but confirmed influenza was more prevalent in the age group of >65 (18.1%) and 25–34 years (14.6%).

Contrary to the present study, in which no difference was observed in the gender of patients with influenza,
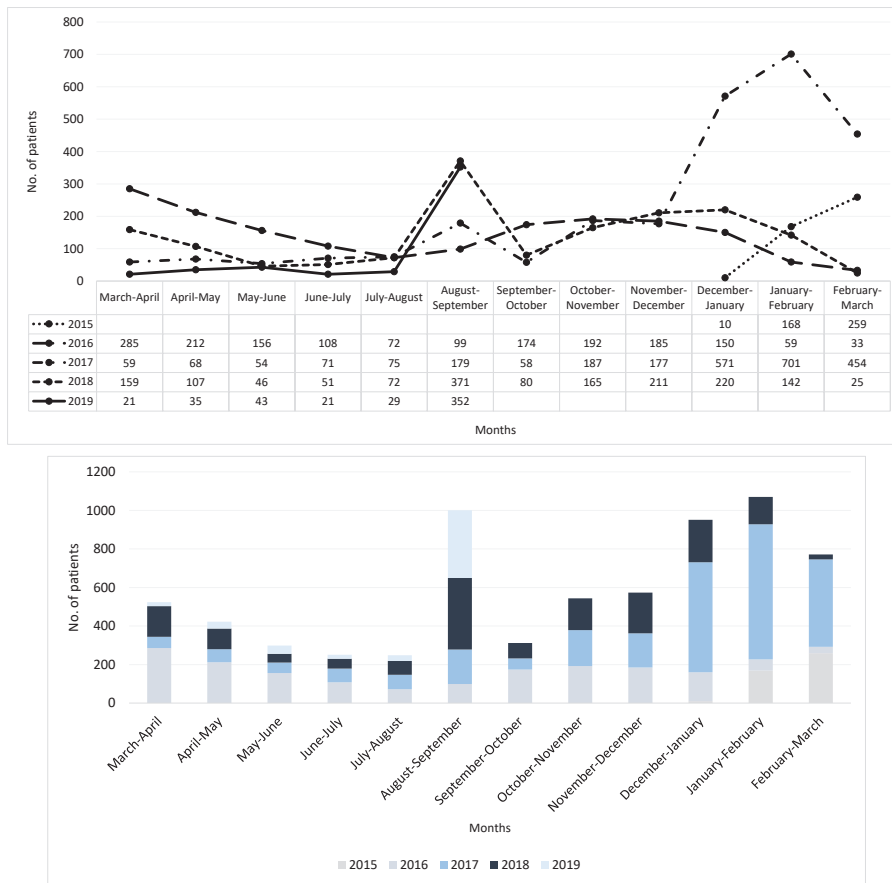
	March-April	April-May	May-June	June-July	July-August	August-September	September-October	October-November	November-December	December-January	January-February	February-March
2015										10	168	259
2016	285	212	156	108	72	99	174	192	185	150	59	33
2017	59	68	54	71	75	179	58	187	177	571	701	454
2018	159	107	46	51	72	371	80	165	211	220	142	25
2019	21	35	43	21	29	352						

Figure 1. Annual Trend of Influenza-Like Illness (ILI) in Southern Iran (2015–2019).

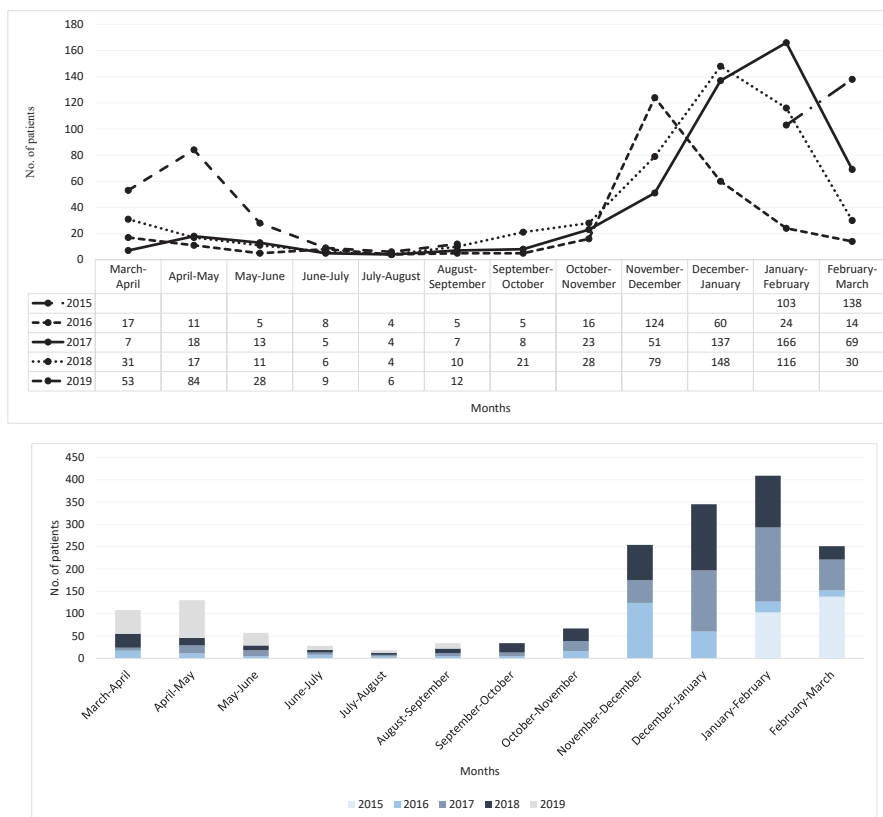|	March-April	April-May	May-June	June-July	July-August	August-September	September-October	October-November	November-December	December-January	January-February	February-March
2015											103	138
2016	17	11	5	8	4	5	5	16	124	60	24	14
2017	7	18	13	5	4	7	8	23	51	137	166	69
2018	31	17	11	6	4	10	21	28	79	148	116	30
2019	53	84	28	9	6	12						

Figure 2. Annual Trend of Severe Acute Respiratory Infections/Illness (SARI) in Southern Iran (2015–2019).

Table 2. Characteristics of Patients Suspected of Influenza with Influenza Sample Test (Unconfirmed) in Southern Iran (2015–2019)

Variables	Patients with Influenza Sample Test (Unconfirmed) (n = 1269)
Age (mean ± SD)	29.40 ± 26.91
Male	28.31 ± 26.89
Female	30.41 ± 26.90
P value	0.94 (95% CI = 1.511,-5.061)
Age groups (%)	
0–1	299 (23.6)
2–4	86 (6.8)
5–14	132 (10.4)
15–24	76 (6.0)
25–34	168 (13.2)
35–44	131 (10.3)
45–54	87 (6.9)
55–64	115 (9.1)
>65	175 (13.8)
Gender (%)	
Male	613 (48.3)
Female	656 (51.7)
P value	0.73
Season of disease (%)	
Spring	220 (17.3)
Summer	83 (6.5)
Autumn	257 (20.3)
Winter	709 (55.9)
Months of disease (%)	
March-April	82 (6.5)
April-May	73 (5.8)
May-June	65 (5.1)
June-July	29 (2.3)
July-August	12 (0.9)
August-September	42 (3.3)
September-October	27 (2.1)
October-November	86 (6.8)
November-December	144 (11.3)
December-January	260 (20.5)
January-February	298 (23.5)
February-March	151 (11.9)
History of travel (%)	
International	70 (5.5)
Domestic	43 (3.39)
History of contact with birds (%)	38 (2.99)
Associated symptoms (%)	
Fever	871 (68.6)
Dyspnea	395 (31.1)
Sore throat	357 (28.1)
Hypotension	298 (23.5)
Cough	281 (22.1)
Hemoptysis	239 (18.8)
Chest discomfort	138 (10.9)
Comorbidities (%)	
Chronic heart diseases	179 (14.1)
Diabetes	97 (7.6)
Chronic pulmonary diseases	70 (5.5)
Chronic nervous diseases	57 (4.5)
Chronic kidney diseases	44 (3.5)
Pregnancy	41 (3.2)
Malignancy	27 (2.1)
Chronic liver diseases	20 (1.6)
Chronic blood diseases	16 (1.3)
Severe obesity	15 (1.2)
Malnutrition	3 (0.2)
HIV/AIDS	3 (0.2)
Without underlying diseases	817 (64.4)

Table 2. Continued

Variables	Patients with Influenza Sample Test (Unconfirmed) (n = 1269)
Laboratory sample (%)	
Total sample	1269
Throat swab	957 (75.41)
Nasal swab	66 (5.20)
Endotracheal suction	151 (12.0)
Not determined	95 (7.49)
Laboratory result (%)	
Positive	204 (16.08)
Negative	724 (57.05)
Not determined	341 (26.87)
Virus type (%)	
A	191 (15.05)
A (H1N1/p)	34 (2.68)
A (H3N2)	58 (4.57)
Other types	1 (0.08)
Not determined	98 (7.72)
B	8 (0.63)
Not determined	5 (0.39)
Complications (%)	
Pneumonia	377 (29.7)
ARDS	84 (6.6)
Cardiopulmonary	62 (4.9)
Bronchitis	55 (4.3)
Neurologic	39 (3.1)
Without complications	769 (60.6)
Patients' outcome (%)	
Outpatients	387 (30.5)
Inpatients	848 (66.8)
Death	34 (2.7)

* Statistically significant; ARDS, acute respiratory distress syndrome; HIV/AIDS, human immunodeficiency viruses/acquired immunodeficiency syndrome

Javid Khojasteh et al, in their study on the prevalence of influenza A/N1H1 in the Guilan province, north of Iran, showed that most patients were females with a mean age of 40 years. The highest prevalence in their study pertained to the age group of 10–20 years, which is not consistent with the results of the present study.[12] Also, Haghshenas et al showed that the age group of 21–30 years constituted more than 50% of influenza A/H3N2 patients in the Guilan province from 2011 to 2013.[13] Rahmanian et al, showed that the age group of 15–40 years constituted the most influenza cases in Jahrom, Iran,[14] and Yavarian et al reported that the highest prevalence pertained to the age group of 20–49 years, which is not in line with the results of the current study.[15] Ling et al in Singapore reported that the majority of the patients belonged to the age group of 38-91 years with a mean age of 91, 10% of whom were males.[16] In a study by Afrasiabian et al, a similar mean age was reported in patients with influenza.[8] The incidence of influenza at the two ends of the age range may be due to a weak immune system; these two age groups need more surveillance and follow-up during an outbreak.

Influenza epidemics mostly occur during winter in temperate regions and during the rainy months of the year in tropical regions, but seasonal trends in epidemics are
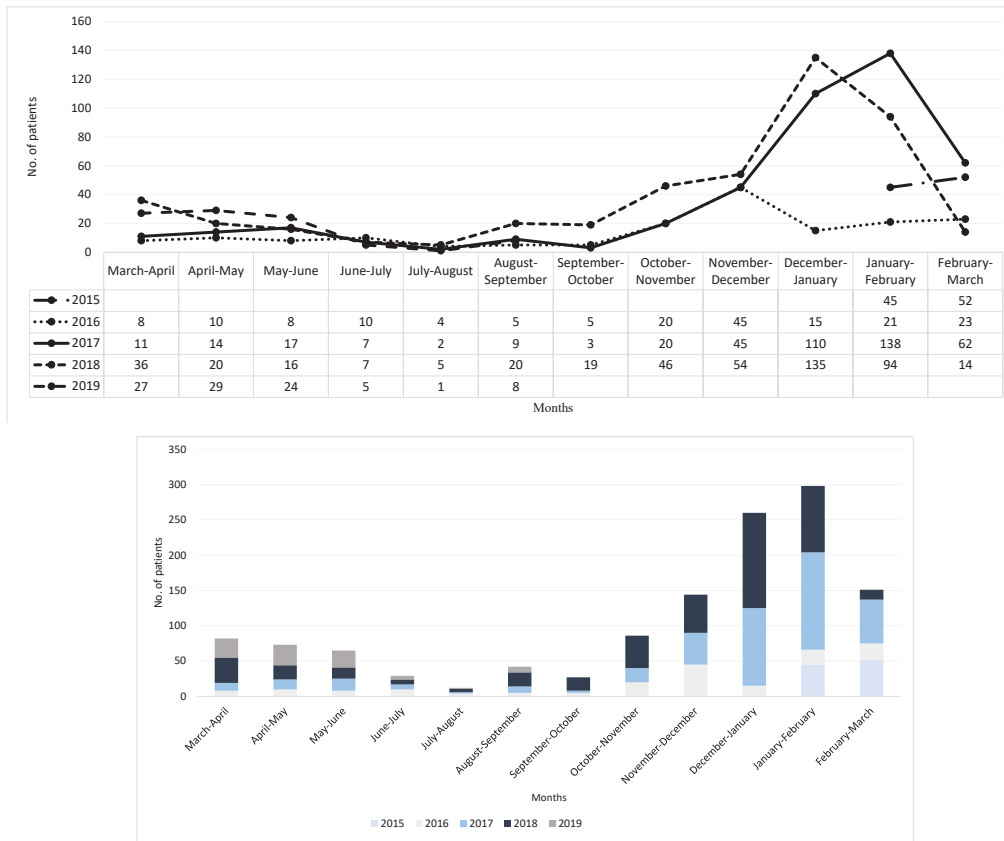
	March-April	April-May	May-June	June-July	July-August	August-September	September-October	October-November	November-December	December-January	January-February	February-March
2015											45	52
2016	8	10	8	10	4	5	5	20	45	15	21	23
2017	11	14	17	7	2	9	3	20	45	110	138	62
2018	36	20	16	7	5	20	19	46	54	135	94	14
2019	27	29	24	5	1	8						

Figure 3. Annual Trend of Unconfirmed Influenza in Southern Iran (2015–2019).

not always constant, and sporadic cases or outbreaks may occur at any place regardless of the season.[17] For example, Zaman et al stated that influenza activity is seasonal and in Bangladesh, most positive samples occurred from June to September.[18] Our results showed that between March-April and June-July, influenza had a decreasing trend, followed by an increase in December-January and January-February (in winter) that reached its peak and then declined. The number of patients had a small increase in August-September. During the study years, the majority of the cases occurred in winters. The findings of Moghaddami et al showed that influenza had two waves; one about a month after the emergence of the disease, and the other, about one month after the reopening of schools. The first peak was predominantly among adults with a history of international travel, while the second was predominantly among school students.[19] Moasser et al also showed that most cases occurred in February and March.[20] Gouya et al reported that influenza is on the rise in the second half of the year coinciding with the reopening of schools and universities.[21] Belderok et al showed that traveling has an effect on the epidemiology of influenza.[23]

Also, our results indicated a downward trend for ILI from February-March to June-July, reaching a peak in August-September, and then decreasing. After that, it is followed by an upward trend that peaks in January-February. In SARI, a small peak was seen in May. A total of 17.05% of

the ILI patients and 15.65% of the SARI were positive for influenza. As influenza virus is one of the most important causes of ILI and SARI,[22] the peak in September may be due to the start of the cold season and also increases in travels to this province, as well as preparing for schools and universities, and after that, it decreases with the start of influenza vaccination and development of herd immunity.

Ziyaeyan et al showed that the frequency of influenza type A in Shiraz, Iran was 4.2%.[24] Haghshenas et al showed that the frequency of influenza type B in the Mazandaran Province, northern Iran was 5.58% from 2011 to 2013.[25] Javid et al reported the prevalence of A/H1N1, A/H3N2, and B influenza at 2.7%, 2.8%, and 3.2%, respectively in the Golestan Province, Iran from 2010 to 2014.[11] In the study by Afrasiabian et al, A/H1N1 was confirmed in 14.8% of the patients.[8] Mozhgani et al, in a meta-analysis on the prevalence of influenza in the Middle East, reported an overall prevalence of 10.2%, which was lower than the results of the present study.[6] The results of the current study showed that 15.05% of the patients had influenza type A, which is higher than those reported in similar studies. Among patients with definite influenza A, 2.68% had H1N1/p subtype and 4.57% had H3N2. It was also found that 0.63% had influenza type B, which is lower than the results of the aforementioned studies.

The current study found that the most commonly prescribed drugs were ceftriaxone and vancomycin, which

Table 3. Difference between Patients with Confirmed Influenza Virus Type A or B in Southern Iran (2015–2019)

Variables	Patients with Confirmed Influenza (n = 199)	Patients with Confirmed Influenza Type A (n = 191)	Patients with Confirmed Influenza Type B (n = 8)	P Value
Age (Mean±SD)	35.85 ± 26.92	35.27 ± 26.81	49.88 ± 27.46	0.133 (95% CI = -33.70, 4.489)
Age groups (%)				
0–1	26 (13.1)	26 (13.6)	0 (0)	
2–4	14 (7.0)	14 (7.3)	0 (0)	
5–14	21 (10.6)	20 (10.5)	1 (12.5)	
15–24	9 (4.5)	9 (4.7)	0 (0)	
25–34	29 (14.6)	27 (14.1)	2 (25.0)	0.422
35–44	25 (12.6)	25 (13.1)	0 (0)	
45–54	18 (9.0)	16 (8.4)	2 (25.0)	
55–64	21 (10.6)	21 (11.0)	0 (0)	
>65	36 (18.1)	33 (17.3)	3 (1.5)	
Gender (%)				
Male	103 (51.8)	101 (52.9)	2 (25.0)	
Female	96 (48.2)	90 (47.1)	6 (75.0)	0.158
P value	0.713	0.497	<0.0001*	
History of travel (%)				
International	10 (5.0)	10 (5.03)	0 (0)	0.848
Domestic	7 (3.5)	6 (3.14)	1 (12.5)	0.668
History of contact to birds (%)	5 (2.5)	5 (2.62)	0 (0)	0.491
Comorbidities (%)				
Chronic heart diseases	31 (15.6)	29 (15.2)	2 (25)	0.362
Diabetes	20 (10.1)	19 (9.9)	1 (12.5)	0.578
Chronic pulmonary diseases	17 (8.5)	16 (8.4)	1 (12.5)	0.517
Chronic nervous diseases	9 (4.5)	9 (4.7)	0 (0)	1.0
Chronic liver diseases	6 (3.0)	6 (3.1)	0 (0)	1.0
Chronic kidney diseases	5 (2.5)	5 (2.6)	0 (0)	1.0
Pregnancy	5 (2.5)	4 (2.1)	1 (12.5)	0.187
Malignancy	2 (1.0)	1 (0.5)	1 (12.5)	0.79
Severe obesity	2 (1.0)	2 (1.0)	0 (0)	1.0
Chronic blood diseases	1 (0.5)	1 (0.5)	0 (0)	1.0
Malnutrition	1 (0.5)	1 (0.5)	0 (0)	1.0
HIV/AIDS	0 (0)	0 (0)	0 (0)	-
Without underlying diseases	118 (59.3)	115 (60.2)	3 (37.5)	0.275
Complications (%)				
Pneumonia	60 (30.2)	59 (30.9)	1 (12.5)	0.439
ARDS	14 (7.0)	14 (7.3)	0 (0)	1.0
Cardiopulmonary	7 (3.5)	7 (3.7)	0 (0)	1.0
Bronchitis	7 (3.5)	7 (3.7)	0 (0)	1.0
Neurologic	3 (1.5)	3 (1.6)	0 (0)	1.0
Without complications	123 (61.8)	116 (60.7)	7 (87.5)	0.158
Prescribed drugs				
Ceftriaxone	57 (28.6)	53 (27.7)	4 (50.0)	0.229
Vancomycin	35 (17.6)	35 (18.3)	0 (0)	0.355
Meropenem	31 (15.6)	31 (16.2)	0 (0)	0.613
Azithromycin	18 (9.0)	17 (8.9)	1 (12.5)	0.538
Amikacin	4 (2.0)	4 (2.1)	0 (0)	1.0
Imipenem	3 (1.5)	3 (1.6)	0 (0)	1.0
Patients' outcome (%)				
Outpatients	62 (31.2)	60 (31.4)	2 (25.0)	0.9947
Inpatients	131 (65.8)	125 (65.4)	6 (75.0)	0.857
Death	6 (3.0)	6 (3.1)	0 (0)	0.578

ARDS, Acute respiratory distress syndrome; HIV/AIDS, human immunodeficiency viruses/ acquired immunodeficiency syndrome

might be due to complications, especially pneumonia. Mozhgani et al reported that the most commonly prescribed drugs for patients with influenza were amantadine, zanamivir, and oseltamivir.[6] Ziyaeyan et al found that all patients with A/H1N1 were sensitive to oseltamivir.[24]

In the present study, 31.2% of patients were hospitalized, which was lower than the rate reported by Afrasiabian et al, and higher than that reported by Cutter et al.[7,8] Unnecessary hospitalization results in financial and human resources losses in the healthcare systems; hence, physicians should be trained on the diagnosis of influenza in order to prevent unnecessary referrals. Also, the results of the current study showed that mortality in patients with definite influenza was 3.0%, and there was no difference between types A and B in this regard. This

Table 4. Association between Complications and Gender, Age Groups, History of International and Domestic Travel, as well as History of Contact with Birds in Patients with Influenza

Variables	Complications					P Value
	Pneumonia (n = 377)	ARD (n = 84)	Bronchitis (n = 55)	Cardiopulmonary (n = 62)	Neurologic (n = 39)	
Gender (%)						
Male	167 (44.3)	44 (52.4)	24 (43.6)	42 (67.6)	20 (51.3)	0.011*
Female	210 (55.7)	40 (47.6)	31 (56.4)	20 (32.3)	19 (48.7)	
P value	0.063	0.439	0.479	0.002*	0.706	
Age groups (%)						
0–1	142 (37.3)	16 (19.0)	30 (54.5)	18 (29.0)	17 (43.6)	
2–4	24 (6.4)	9 (10.7)	2 (3.6)	2 (3.2)	3 (7.7)	
5–14	48 (12.7)	6 (7.1)	9 (16.4)	5 (8.1)	8 (20.5)	
15–24	15 (4.0)	6 (7.1)	1 (1.8)	7 (11.3)	2 (5.1)	
25–34	32 (8.5)	7 (8.3)	1 (1.8)	2 (3.2)	3 (7.7)	0.290
35–44	24 (6.4)	11 (13.1)	3 (5.5)	9 (14.5)	3 (7.7)	
45–54	18 (4.8)	7 (8.3)	1 (1.8)	3 (4.8)	1 (2.6)	
55–64	23 (6.1)	7 (8.3)	3 (5.5)	7 (11.3)	2 (5.1)	
>65	51 (13.5)	15 (17.9)	5 (9.1)	9 (14.5)	0 (0)	
P value	<0.0001*	0.466	<0.0001*	0.14	0.123	
History of international travel (%)						
Yes	19 (5.0)	3 (3.6)	1 (1.8)	6 (9.7)	0 (0)	0.152
No	358 (95.0)	81 (96.4)	54 (98.2)	56 (90.3)	39 (100)	
P value	0.629	0.619	0.361	0.141	0.129	
History of domestic travel (%)						
Yes	13 (3.4)	3 (3.6)	4 (7.3)	3 (4.8)	2 (5.1)	0.720
No	364 (96.6)	81 (96.4)	51 (92.7)	59 (95.2)	37 (94.9)	
P value	0.939	0.759	0.111	0.463	0.384	
History of contact with birds (%)						
Yes	6 (1.6)	3 (3.6)	2 (3.6)	1 (1.6)	1 (2.6)	0.718
No	371 (98.4)	81 (96.4)	53 (96.4)	61 (98.4)	38 (97.4)	
P value	0.057	0.619	0.679	1.0	1.0	

* Statistically significant.

Table 5. Outcome of Patients with Confirmed Influenza in Southern Iran (2015–2019)

Age Groups	Outpatients (%)	Inpatients (%)	Death (%)	Total (%)	P Value
0-1	16 (12.2)	10 (16.1)	0 (0)	26 (13.1)	
2-4	9 (6.9)	5 (8.1)	0 (0)	14 (7.0)	
5-14	17 (13.0)	4 (6.5)	0 (0)	21 (10.6)	
15-24	7 (5.3)	2 (3.2)	0 (0)	9 (4.5)	
25-34	17 (13.0)	11 (17.7)	1 (16.7)	29 (14.6)	0.036*
35-44	18 (13.7)	3 (4.8)	4 (66.7)	25 (12.6)	
45-54	13 (9.9)	5 (8.1)	0 (0)	18 (9.0)	
55-64	10 (7.6)	10 (16.1)	1 (16.7)	21 (10.6)	
>65	24 (18.3)	12 (19.4)	0 (0)	36 (18.1)	
Total	131 (65.8)	62 (31.2)	6 (3.0)	199	

* Statistically significant.

rate was reported at 3.8% by Gouya et al.[21] The mortality rate in the current study was higher than the reported results of Haghshenas et al and Yavarian et al.[15,26] Contrary to the results of the present study, Mozhgani et al reported that A/H1N1 had the highest mortality than the other subtypes.[6] The reported mortality rate of A/H1N1 is even lower in some countries.[27-29]

The results of the current study showed that fever and dyspnea were the most frequent symptoms associated with influenza. The results of various studies show that the frequency of symptoms is different. Most studies reported fever and cough as the most common symptoms.[14,18,27,29] Also, our result indicated that chronic heart disease and diabetes were the most prevalent comorbidities in our patients, but Yacarian et al reported asthma and diabetes, as well cardiovascular disease as the most common underlying diseases in patients who expired.[15]

The strength of our study is using a large database, the Syndromic Surveillance System of Iran's health ministry, which records data from all patients who were referred to one of the Health Centers in the Fars province. Lack of complete records of patients' information in this system

was one of the limitations of the current study. As this disease is self-limited in most of the patients,[8] a large proportion of infected population are not registered in health centers and the statistical estimation may not perfectly reflect the reality.

In conclusion, the results showed that the incidence of influenza, especially type A in the Fars province, southern Iran is considerable and requires more attention for prevention in health policy programs.

Supplementary Materials
Supplementary file 1 contains Table S1.

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