Clinical Symptoms of COVID-19 and Their Association with Disease Outcome

Abstract

**Background**: COVID-19 pandemic placed immense pressure on health systems. The current study aimed to evaluate the symptoms of COVID-19 in Isfahan province and their association with disease outcome. **Materials and Methods**: In this cross-sectional study, which was conducted on patients with a definite diagnosis of COVID-19, as a part of the investigations performed by the Deputy for Public Health of the Isfahan University of Medical Sciences, the frequency of underlying diseases, and general, respiratory, gastrointestinal, neurological, renal, cardiac, dermal, hearing symptoms are assessed using a checklist. The participants were followed up 1 month after definitive diagnosis, and the outcome of the disease (recovery or death) was recorded. **Results**: Of 300 patients, 143 (47.4%) were male and 157 (52.6%) were female. The mean age of patients was 43 ± 17.84 years. Muscle pain and fatigue were the most common early symptoms (63% and 60.3%, respectively). Age, sex, level of education, and occupation of patients and general, respiratory, and gastrointestinal symptoms and underlying diseases of respiratory disease showed a statistically significant association with the disease outcome (P < 0.05). **Conclusion**: General, respiratory, and gastrointestinal symptoms were associated with an increased risk of death due to COVID-19. General, visual, and hearing symptoms, and diabetes, cardiovascular diseases, and respiratory disease had a statistically significant association with the hospitalization of patients.

**Keywords**: Signs and Symptoms, COVID-19, death, hospitalization

Introduction

Similar to other countries, the COVID-19 pandemic is a serious public health challenge in Iran also. The most important clinical symptoms of COVID-19 patients are fever, cough, sputum, headache, vomiting, diarrhea, fatigue, rhinorrhea, and chest pain, among which fever, cough, and dyspnea are the most frequent manifestations. Awareness about the prevalence of these symptoms is key for the identification and primary screening of patients.

Several preliminary studies have investigated the prevalence of fever and cough in COVID-19 patients. For instance, Shi et al. reported a prevalence of 72.8% for fever and 59.2% for cough. Tian et al. reported a prevalence of 82% and 45.8% for fever and cough, respectively. Furthermore, in the study by Song et al., the prevalence of fever and cough is reported as 96% and 47%, respectively. Hence, it can be argued that various studies have reported different rates of prevalence for fever and cough, as the most common symptoms of COVID-19.

According to the British Medical Journal, the most common diagnostic symptoms of COVID-19 include fever (83%–98%), which may be associated with shivering, dry cough (57%–82%), dyspnea (18%–55%), which its median duration is 5–8 days after the infection, decreased or lost sense of smell in patients with mild to moderate disease, 86% of patients had anosmia. The American Ear, Nose, Throat Association and the American Academy of Otolaryngology–Head and Neck Surgery recommended that COVID-19 screening programs should consider these two symptoms (i.e., fever and cough) as the most important criteria. Other symptoms include conjunctivitis, gastrointestinal symptoms, dizziness, confusion, headache, weakness, and
myalgia or muscle pain, anorexia that usually manifests in the early stages of the disease. A systematic review by Kazemnia et al. in Iran (February 2020) reported a high prevalence of fever and cough in COVID-19 patients. They also mentioned that these symptoms increase with age.

Various studies have described the clinical manifestations of COVID-19, but data on the association of these symptoms and clinical manifestations with disease outcome are scarce.

As new symptoms are identifying for COVID-19, in addition to previously identified symptoms (i.e., fever, cough, sore throat, and dyspnea), the purpose of this study is to firstly investigate the symptoms of COVID-19 in Isfahan province of Iran and secondly examining their association with outcome of the disease.

Materials and Methods

This cross-sectional study was conducted on patients with a definite diagnosis of COVID-19, as a part of the investigations performed by the Deputy for Public Health of the Isfahan University of Medical Sciences since May 2020. Inclusion criteria were new positive polymerase chain reaction (PCR) test results and consent to participate in the study. The exclusion criteria included incomplete information as well as patient's death before the study started or during the recruitment period. The current study is approved by the Ethics Committee of the Isfahan University of Medical Sciences (code: IR.MUI.MED.REC.1399.312).

To calculate the sample size, taking into account the statistical confidence interval (CI) of 95% and the prevalence of cough 45% and statistical accuracy of 0.07, the sample size of 217 people was calculated, taking into account the attrition rate, the final sample size was 300 people. Using the Excel software, 300 COVID-19 newly diagnosed patients were randomly selected from the list of COVID-19 patients living in various regions of the province. Then, a questioner in selected outpatient and inpatient health-care centers filled the study checklist, which included demographic characteristics of people (i.e., age, gender, education and occupation, place of residence), underlying disease, general symptoms as well as respiratory, gastrointestinal, neurological, kidney, hearing, vision, smell, heart, and skin symptoms. The participants were followed up 1 month after definitive diagnosis by phone, and the outcome of the disease (recovery, death, and need for hospitalization) was recorded.

Numerical variables are reported as mean and standard deviation, while qualitative variables are described as frequency and percentage. Chi-square and Fisher’s exact tests were used to analyze qualitative variables, and simple and multiple logistic regressions were used to investigate the association between factors that predict patients’ outcomes. Variables that were significant in univariate correlations were entered into the multiply regression analysis. Logistic regression results are reported as odds ratio (OR) using a 95% CI. Data were analyzed using Statistical Package for Social Sciences (SPSS Inc., Chicago, Illinois, USA) version 23. Statistical significance was considered when \( P < 0.05 \).

Results

Of 332 invited patients, 300 responded for a return rate of 90.3%, 143 (47.4%) were male, and 157 (52.6%) were female with a mean age of 43 ± 17.48 years. The median age of participants was 40 years. The youngest and oldest participants were 2 and 93 years old, respectively. The highest death rate (28%) was observed in the age group of 30–40 years. The highest case fatality rate (46.2%) was in the age group of over 80 years. Both mortality and fatality rates were higher in males than females (81.8% vs. 18.2% and 6.3% vs. 1.3%, respectively). All deaths were among those living in urban areas and the highest death rate was among those educated up to diploma. Furthermore, 11 (3.7%) patients died and 67 (22.3%) were hospitalized. Besides, no death was observed among outpatients.

Concerning underlying diseases, diabetes was the most common disease (\( n = 35 \) or 11.7%), followed by cardiovascular diseases (CVDs) (\( n = 27 \) or 9%), pulmonary disease (\( n = 16 \) or 5.3%), and obese and overweight (\( n = 146 \) or 55.5%).

Three patients (2.1%) were pregnant. Information on demographic characteristics, underlying diseases, and death rate, and fatality rate are described in Table 1. In the present study, 276 (92%) patients presented general symptoms, 211 (70.3%) had respiratory symptoms, 48 (16%) had skin symptoms, 104 (34.7%) had ocular symptoms, 49 (16.3%) had hearing symptoms, 6 (2%) had breast symptoms, 150 (50%) had cardiovascular symptoms, 161 (53.7%) had gastrointestinal symptoms, 72 (24%) had renal symptoms, and 198 (66%) had neurological symptoms. Muscle weakness (63%) and pain (60.3%) were the most common primary symptoms, followed by fever, shivering, and cough. Other clinical symptoms are listed in Table 2.

There was a significant association between demographic characteristics (i.e., age, gender, education level, and occupation of patients) and primary symptoms of the disease (i.e., general symptoms, respiratory, and gastrointestinal symptoms) and underlying diseases (i.e., respiratory diseases) \( (P < 0.05) \). The mean age of COVID-19 patients who died was significantly higher than survived patients \( (77.5 \pm 10.4 \text{ vs. } 41.7 \pm 16.7, \text{respectively}; P < 0.00001) \). Other information related to the association between mortality and recovery of patients and demographic characteristics and primary symptoms of patients is provided in Table 3. There was a significant association between demographic characteristics of patients, education
level, and primary symptoms of general, ocular, and hearing and underlying diseases of diabetes, CVDs, and respiratory diseases \( (P < 0.05) \). The association between underlying diseases and history of influenza vaccination in patients with COVID-19 and hospitalization status and outcome of the disease is provided in Table 4. The results of logistic regression are described in Table 5. These findings revealed that patients with respiratory diseases are at increased risk of hospitalization and death. However, after adjusting the effect of age and gender variables, the association was not significant. The OR was higher for patients with underlying diseases of diabetes, CVDs, respiratory diseases, and liver

| Table 1: Demographic and clinical characteristics and mortality status of patients with coronavirus disease 2019 \( (n=300) \) |
|-----------------|-----------|---------|------------|
| Variable        | Frequency (%) | Death (%) | Fatality rate (%) |
| Population      | 300       | 11      | 3.7        |
| Age             |           |         |            |
| 0-10            | 8 (2.7)   | 0       | 0          |
| 10-20           | 15 (5.1)  | 0       | 0          |
| 20-30           | 46 (15.5) | 0       | 0          |
| 30-40           | 83 (28)   | 0       | 0          |
| 40-50           | 57 (19.3) | 0       | 0          |
| 50-60           | 37 (12.5) | 1 (9.1) | 2.7        |
| 60-70           | 27 (9.1)  | 2 (18.2)| 7.4        |
| 70-80           | 10 (3.4)  | 2 (18.2)| 20         |
| >80             | 13 (4.4)  | 6 (54.5)| 46.2       |
| Gender          |           |         |            |
| Female          | 157 (52.3)| 2 (18.2)| 1.3        |
| Male            | 143 (47.7)| 9 (81.8)| 6.3        |
| Residence area  |           |         |            |
| Urban           | 282 (95.9)| 11 (100)| 3.9        |
| Rural           | 12 (4.1)  | 0       | 0          |
| Education       |           |         |            |
| Illiterate      | 12 (4.2)  | 3 (33.3)| 25         |
| Less than diploma | 102 (35.9)| 5 (55.6)| 4.9        |
| Diploma         | 66 (23.2) | 1 (11.1)| 1.5        |
| University degree | 104 (36.6)| 0       | 0          |
| Services        |           |         |            |
| Outpatient      | 233 (77.7)| 0       | 0          |
| Inpatient       | 67 (22.3) | 11 (100)| 16.4       |
| Underlying diseases |       |         |            |
| Cancer          | 4 (1.3)   | 0       | 0          |
| Diabetes        | 35 (11.7) | 2 (18.2)| 5.7        |
| Cardiovascular diseases | 27 (9)   | 2 (18.2)| 7.4        |
| Pulmonary diseases | 16 (5.3) | 4 (36.4)| 1.9        |
| Liver diseases  | 11 (3.7)  | 1 (9.1) | 9.1        |
| Renal disease   | 11 (3.7)  | 0       | 0          |
| Organ transplantation | 2 (0.7) | 0       | 0          |
| Pregnant        | 3 (2.1)   | 0       | 0          |
| BMI             |           |         |            |
| Underweight     | 14 (5.3)  | 1 (20)  | 7.1        |
| Normal          | 103 (39.2)| 1 (20)  | 1          |
| Overweight and obesity | 146 (55.5)| 3 (60)  | 2.1        |

BMI: Body mass index

| Variable                  | Frequency (%) |         |
|---------------------------|--------------|---------|
| General symptoms          |              |         |
| Fever                     | 159 (53)     |         |
| Chills                    | 165 (55)     |         |
| Weakness                  | 189 (63)     |         |
| Confusion                 | 117 (37.3)   |         |
| Muscle pain               | 181 (60.3)   |         |
| Joint pain                | 88 (29.3)    |         |
| Decreased appetite        | 124 (41.3)   |         |
| Reduced sense of smell    | 121 (40.3)   |         |
| Reduced taste sense       | 86 (28.7)    |         |
| Night sweating            | 126 (42)     |         |
| Pulmonary symptoms        |              |         |
| Shortness of breath       | 117 (39)     |         |
| Throat ulcers             | 93 (31)      |         |
| Cough                     | 147 (49)     |         |
| Runny nose                | 50 (16.7)    |         |
| Skin symptoms             |              |         |
| Bruising of the skin      | 3 (1)        |         |
| Rash                      | 16 (5.3)     |         |
| Wounds                    | -            |         |
| Itching                   | 27 (9)       |         |
| Urticaria                 | 11 (3.7)     |         |
| Skin discoloration        | 1 (0.3)      |         |
| Dry skin                  | 9 (3)        |         |
| Ocular symptoms           |              |         |
| Tearful                   | 9 (3)        |         |
| Secretion from the eye    | 1 (0.3)      |         |
| Red eye                   | 48 (16)      |         |
| Eye pain                  | 27 (9)       |         |
| Blurred vision            | 35 (11.7)    |         |
| Hearing symptoms          |              |         |
| Hearing loss              | 17 (5.7)     |         |
| Tinnitus                  | 13 (4.3)     |         |
| Ear pain                  | 24 (8)       |         |
| Ear infection             | 3 (1)        |         |
| Ear secretion             | 2 (0.7)      |         |
| Cardiac symptoms          |              |         |
| Chest pain                | 92 (30.7)    |         |
| Palpitation               | 72 (24)      |         |
| Shortness of breath during rest | 78 (26) |         |
| Shortness of breath during night | 11 (3.7) |         |
| Gastrointestinal symptoms |              |         |
| Difficulty swallowing     | -            |         |
| Heartburn                 | 3 (1)        |         |
| Pain during swallowing    | 1 (0.3)      |         |
| Nausea                    | 67 (22.3)    |         |
| Vomiting                  | 21 (7)       |         |
| Diarrhea                  | 98 (32.7)    |         |
| Constipation              | 9 (3)        |         |
| Abdominal pain            | 44 (14.7)    |         |
| Lingering                 | 2 (0.7)      |         |
| Renal symptom             |              |         |
| Back pain                 | 2 (0.7)      |         |

Contd...
This difference can be attributed to using various factors such as genetics, method of transmission, viral load, and other factors. The study by Bagheri et al., in a study on 10,069 patients, mentioned that 60.9% of patients reported smell loss. In the present study, 40.3% of patients experienced smell loss. This finding is consistent with the study by Nikpouraghdam et al., which investigated patients admitted to Baqiyatallah Hospital in Tehran.

Bagheri et al., in a study on 10,069 patients, mentioned weakness and fever as the most common symptoms of COVID-19. In a study on 1099 patients with COVID-19, 43.8% of patients presented fever at the initial stage of the disease, which in the present study, it was about 50%. A review study by Jiang et al. in China reported that the most common symptom in all studies was fever (more than 90%), followed by cough. While in the present study, muscle weakness and pain were the most common symptoms, and fever, shivering, and cough were other common symptoms. This difference can be attributed to the fact that in the present study, symptoms were recorded through self-reporting, and the patients usually have a lower fever; hence, probably the patients underreported their fever. In the present study, the highest death rate was observed in the age group over 80 years and men. This finding is consistent with the study by Nikpouraghdam et al., which investigated patients admitted to Baqiyatallah Hospital in Tehran.

Discussion

In the present study, 300 patients with a definitive diagnosis of COVID-19, using the PCR test, were investigated. The most common symptom was general symptoms, most notably muscle weakness and pain. In a study conducted in China, Zhou et al. mentioned weakness and fever as the most common symptoms of COVID-19. In a study on 1099 patients with COVID-19, 43.8% of patients presented fever at the initial stage of the disease, which in the present study, it was about 50%. A review study by Jiang et al. in China reported that the most common symptom in all studies was fever (more than 90%), followed by cough. While in the present study, muscle weakness and pain were the most common symptoms, and fever, shivering, and cough were other common symptoms. This difference can be attributed to the fact that in the present study, symptoms were recorded through self-reporting, and the patients usually have a lower fever; hence, probably the patients underreported their fever. In the present study, the highest death rate was observed in the age group over 80 years and men. This finding is consistent with the study by Nikpouraghdam et al., which investigated patients admitted to Baqiyatallah Hospital in Tehran.

The risk of death from COVID-19 was higher in men and those older than 65 years, which is consistent with the study by Soares et al. in Brazil. In the present study, the OR of death was higher in patients with respiratory diseases, diabetes, CVD, and hepatic disease, which is consistent with the study by Masetti et al. in Italy. Considering that the mean age of deceased patients was higher than those who survived, having CVDs and diabetes were associated with a higher risk of death due to COVID-19 compared to respiratory diseases and liver disorders. The increased risk of death observed in the single variable model was due to the effect of older age. In a meta-analysis by Huang et al., diabetes was associated with an increased relative risk of death due to COVID-19.

Furthermore, in a meta-analysis study conducted on Chinese data, having respiratory diseases was associated with an increased relative risk of death due to COVID-19 by four times; in the present study, it was increased by 7.96 times.

In our study, having more primary symptoms were associated with a reduced risk of death. Besides, having general and respiratory symptoms were associated with a significant increase in the risk of death. Soares et al., in a study conducted in Brazil, reported that having any of the primary symptoms such as cough, fever, and shortness of breath was associated with a significant increase in relative risk of death. In this study, the chance of hospitalization was significantly higher for males and those older than 65 years, which is consistent with the study by Soares. In our study, in univariate analysis, underlying diseases such as diabetes, CVDs, cancer, respiratory disease, and kidney disease, and pregnancy were associated with an increased chance of hospitalization due to COVID-19, which is consistent with the study by Robilotti et al. conducted in the USA. However, in multivariate analysis, after adjusting the effect of age and gender, the chance of hospitalization for patients with diabetes, cancer, respiratory diseases, and pregnancy was still higher which indicates that age and gender affect the chance of hospitalization for patients with underlying diseases of CVDs and renal disease but it was not statistically significant.

Having more primary symptoms was correlated with a reduced risk of hospitalization. Having general symptoms was associated with an increased risk of hospitalization while having visual and hearing symptoms significantly reduced hospitalization rates. In the study by Soares et al., having any of the primary symptoms such as cough, fever, diarrhea had been associated with a decreased chance of hospitalization. This difference can be attributed to using

| Variable | Frequency (%) |
|----------|--------------|
| Breast symptoms | 9 (3.3) |
| Breast mass | 1 (0.3) |
| Breast secretion | - |
| Breast pain | 5 (1.7) |
| Increased alertness | 1 (0.3) |
| Seizure | - |
| Diplopia | 2 (0.7) |
| Neurologic symptom | 15 (5) |
| Motor paralysis | 6 (21) |
| Numbness | 40 (13.3) |
| Pins and needles | 15 (5) |
| Shivering | 40 (13.3) |
| Headache | 155 (51.7) |
| Confusion | 117 (37.3) |
| Breast mass | 1 (0.3) |
| Breast secretion | - |
| Breast pain | 5 (1.7) |
| Urinary irritation | 15 (5) |
| Frequent urination | 63 (21) |
| Urinary urgency | - |
| Urinary incontinence | 2 (0.7) |
The current study had limitations, including a relatively small sample size, which resulted in a small number of

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**Table 3: The association between demographic characteristics and primary symptoms in patients with coronavirus disease 2019 with hospitalization status and disease outcome (n=300)**

| Demographic characteristics and Primary symptoms | Hospitalization, N (%) | P* | Diseases outcome, N (%) | P* |
|--------------------------------------------------|------------------------|----|-------------------------|----|
|                                                  | Outpatient | Inpatient |                  |                  |
| Gender                                           |            |           |                  |                  |
| Male                                             | 108 (46.4) | 35 (52.5) | 0.39             |
| Female                                           | 125 (53.6) | 32 (47.5) |                  |
| Education level                                  |            |           |                  |                  |
| Illiterate                                       | 4 (1.8)    | 8 (12.7)  | <0.00001**       |
| Less than diploma                                | 67 (30.3)  | 35 (55.6) | 0.02**           |
| Diploma                                          | 54 (24.4)  | 12 (19)   |                  |
| University degree                                | 96 (43.4)  | 8 (12.7)  |                  |
| Occupation                                       |            |           |                  |                  |
| Worker                                           | 51 (23.2)  | 8 (12.9)  | 0.1              |
| Employee                                         | 17 (7.7)   | 4 (6.5)   |                  |
| Self-employed                                    | 37 (16.8)  | 12 (19.4) | 0.01**           |
| Retired                                          | 14 (6.4)   | 10 (16.1) | 0.04**           |
| Unemployed                                       | 87 (39.5)  | 26 (41.9) | 0.003**          |
| Student                                          | 14 (6.4)   | 2 (3.2)   |                  |
| Residence area                                   |            |           |                  |                  |
| Urban                                            | 217 (97)   | 65 (95.6) | >0.99            |
| Rural                                            | 10 (3)     | 2 (4.4)   |                  |
| General symptoms                                 |            |           |                  |                  |
| Yes                                              | 216 (92.7) | 54 (80.6) | 0.004**          |
| No                                               | 17 (7.3)   | 13 (19.4) | 0.73             |
| Pulmonary                                        |            |           |                  |                  |
| Yes                                              | 165 (70.8) | 46 (68.7) | 0.009**          |
| No                                               | 68 (29.2)  | 21 (31.3) | 0.01**           |
| Skin                                             |            |           |                  |                  |
| Yes                                              | 35 (15)    | 13 (19.4) | 0.38             |
| No                                               | 198 (85)   | 54 (80.6) | 0.22             |
| Ocular                                           |            |           |                  |                  |
| Yes                                              | 94 (40.3)  | 10 (14.9) | <0.0001**        |
| No                                               | 139 (59.7) | 57 (85.1) | 0.06             |
| Hearing                                          |            |           |                  |                  |
| Yes                                              | 45 (19.3)  | 4 (6)     | 0.009**          |
| No                                               | 188 (80.7) | 63 (94)   | 0.22             |
| Cardiovascular                                   |            |           |                  |                  |
| Yes                                              | 114 (48.9) | 36 (53.7) | 0.57             |
| No                                               | 119 (51.1) | 31 (46.3) | 0.06             |
| Digestive                                        |            |           |                  |                  |
| Yes                                              | 131 (56.2) | 30 (44.8) | 0.12             |
| No                                               | 102 (43.8) | 37 (55.2) | 0.07             |
| Renal                                            |            |           |                  |                  |
| Yes                                              | 61 (26.2)  | 11 (16.4) | 0.1              |
| No                                               | 172 (73.8) | 56 (83.6) | 0.07             |
| Neuro                                            |            |           |                  |                  |
| Yes                                              | 154 (66.1) | 43 (64.2) | 0.77             |
| No                                               | 79 (33.9)  | 24 (35.8) | 0.52             |
| Breast                                           |            |           |                  |                  |
| Yes                                              | 5 (2.1)    | 1 (1.5)   | 1                |
| No                                               | 228 (97.9) | 66 (98.5) | 1                |

*: P<0.05, **: P<0.01

A self-reported approach for collecting data in the present study.
Table 4: The association between underlying disease and history of influenza vaccination in patients with coronavirus disease 2019 and hospitalization status and outcome (n=300)

| Underlying diseases   | Hospitalization, N (%) | Disease outcome, N (%) | P*  |
|-----------------------|------------------------|------------------------|-----|
|                       | Outpatient | Inpatient | Survival | Death |       |
| Cancer                |            |            |          |       |       |
| Yes                   | 3 (1.3)    | 1 (1.5)    | 4 (1.4)  | 0     | 1     |
| No                    | 230 (98.7) | 66 (98.5)  | 285 (98.6) | 11 (100) |       |
| Diabetes              |            |            |          |       |       |
| Yes                   | 20 (8.6)   | 15 (22.4)  | 33 (11.4) | 2 (18.2) | 0.62  |
| No                    | 231 (91.4) | 52 (77.6)  | 256 (88.6) | 9 (91.8) |       |
| Cardiovascular disease|            |            |          |       |       |
| Yes                   | 15 (6.4)   | 12 (17.9)  | 25 (8.7)  | 2 (18.2) | 0.27  |
| No                    | 218 (93.6) | 55 (82.1)  | 264 (91.3) | 9 (81.8) |       |
| Pulmonary disease     |            |            |          |       |       |
| Yes                   | 9 (3.9)    | 7 (10.4)   | 13 (4.5)  | 3 (27.3) | 0.001**|
| No                    | 224 (96.1) | 60 (89.6)  | 276 (95.5) | 8 (72.7) |       |
| Hepatic disease       |            |            |          |       |       |
| Yes                   | 9 (3.9)    | 2 (3)      | 10 (3.5)  | 1 (9.1)  | 0.34  |
| No                    | 224 (96.1) | 65 (97)    | 279 (96.5) | 10 (90.9) |       |
| Renal disease         |            |            |          |       |       |
| Yes                   | 7 (3)      | 4 (6)      | 11 (3.8)  | 0      | 1     |
| No                    | 226 (97)   | 63 (94)    | 278 (96.2) | 11 (100) |       |
| Organ transplantation |            |            |          |       |       |
| Yes                   | 1 (0.4)    | 1 (1.5)    | 2 (0.7)   | 0      | 1     |
| No                    | 232 (99.6) | 66 (98.5)  | 287 (99.3) | 11 (100) |       |
| Pregnant              |            |            |          |       |       |
| Yes                   | 2 (1.7)    | 1 (96.7)   | 3 (2.1)   | 0      | 1     |
| No                    | 114 (98.3) | 29 (3.3)   | 142 (97.9) | 1 (100) |       |
| BMI                   |            |            |          |       |       |
| Slim                  | 12 (5.5)   | 2 (4.4)    | 13 (5)    | 1 (20)  | 0.27  |
| Normal                | 85 (39.2)  | 18 (39.1)  | 102 (39.5) | 1 (20)  |       |
| Overweight and obese  | 120 (55.3) | 26 (56.5)  | 143 (55.4) | 3 (60)  |       |
| Influenza vaccine     |            |            |          |       |       |
| Yes                   | 17 (7.3)   | 7 (10.4)   | 24 (8.3)  | 0      | 1     |
| No                    | 215 (92.7) | 60 (89.6)  | 264 (91.7) | 11 (100) |       |

*Chi-square test, *: P<0.05, **: P<0.01 BMI: Body mass index

dead and hospitalization events (as the main outcomes) and nonsignificance of associations.

Other limitations were collecting data through self-reporting, which probably has affected the accuracy of the findings. So that, while all studies mentioned fewer as the most common symptom, in the present study, it was the third common symptom.

Conclusion

According to the findings, those older than 65 years, males, and patients with respiratory diseases have an increased chance of death and hospitalization. General symptoms such as muscle weakness and pain and respiratory and gastrointestinal symptoms were associated with an increased risk of death. Meanwhile, general symptoms, and visual and hearing symptoms, and underlying diseases of diabetes, CVDs, and respiratory disease were significantly associated with hospitalization.

Ethics approval

All participants were aware of the objectives of the study and were willing to participate in the study.

All participants were told that their information would be reported in the articles and they expressed their consent.

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The current study is approved by the Ethics Committee of the Isfahan University of Medical Sciences (code: IR.MUI.MED.REC.1399.312). The authors declare no conflict of interest concerning publications of this study.
| Variables                          | Death                  | Hospitalization | Death                  | Hospitalization |
|-----------------------------------|------------------------|-----------------|------------------------|-----------------|
| Age                               | Univariate OR (95% CI) | Multivariate OR (95% CI) |
| <65                               | 1                      | NC              | 1                      | NC              |
| Older than 65                     | 108.75 (13.34-866.03)  | 11.27 (5.1-24.88) | NC                     | NC              |
| Gender                            |                        |                 |                        |                 |
| Female (reference)                | 1                      | NC              | 1                      | NC              |
| Male                              | 5.2 (1.1-24.51)        | 1.26 (0.73-2.18) | NC                     | NC              |
| Diabetes                          | 1.72 (0.35-8.32)       | 3.07 (1.47-6.4)  | 0.46 (0.06-3.13)       | 1.49 (0.65-3.4) |
| Cancer                            | NC                     | 1.16 (0.11-11.35)| NC                     | 2.69 (0.26-27.35)|
| Cardiovascular disease            | 2.34 (0.48-11.46)      | 3.17 (1.47-7.16) | 0.56 (0.08-3.76)      | 0.98 (0.37-2.55) |
| Pulmonary disease                 | 7.96 (1.88-33.56)      | 2.9 (1.03-8.11)  | 2.42 (0.34-17.17)     | 1.61 (0.49-5.30) |
| Hepatic disease                   | 2.79 (0.32-23.95)      | 0.76 (0.16-3.66) | 3.08 (0.1-90.15)      | 0.55 (0.1-2.96)  |
| Renal disease                     | NC                     | 2.05 (0.58-7.22) | NC                     | 0.86 (0.19-3.86) |
| Pregnant                          | NC                     | 1.96 (0.17-22.43)| NC                     | 4.13 (0.33-50.94)|
| BMI                               |                        |                 |                        |                 |
| Normal (reference)                | 1                      | 1               | 1                      | 1               |
| Slim                              | 7.84 (0.46-133.12)     | 0.78 (0.16-3.82) | 17.58 (0.49-624.97)   | 0.97 (0.16-5.94) |
| Overweight and obese              | 2.14 (0.21-20.86)      | 1.02 (0.52-1.98) | 1.13 (0.07-16.84)     | 0.73 (0.35-1.52) |

*Adjusted for age and gender. NC: Not calculable, BMI: Body mass index, OR: Odds ratio, CI: Confidence interval

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### Conflicts of interest
There are no conflicts of interest.

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