Journal of Taibah University Medical Sciences (2022) 17(5), 725–731

Taibah University

Journal of Taibah University Medical Sciences

www.sciencedirect.com

Original Article

COVID-19: Clinical features, case fatality, and the effect of symptoms on mortality in hospitalized cases in Iran

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Received 16 December 2021; revised 2 March 2022; accepted 27 April 2022; Available online 10 May 2022

الملخص

أهداف البحث: تحديد الخصائص الوبائية لهذا المرض يمكن أن يساعد في السيطرة على الوباء. كان الهدف من هذه الدراسة هو توصيف السمات الوبائية لمرضى كوفيد-19 المنومين في المستشفيات في إيران.

طرق البحث: تم استخدام البيانات الخاصة بالمرضى الذين تم إدخالهم إلى مستشفى الإحالة العسكري في طهران، إيران، في الفترة من 8 فبراير 2020 إلى 28 يوليو 2021. تم فحص الجنس والعمر والأعراض السريرية والنتيجة ونوع الأمراض المصاحبة ومستوى الأكسجين في الدم ووقت الدخول ووقت الخروج. كما تم تحديد نسبة الجنس، ومعدل وفيات الحالات، والاتجاه اليومي لدخول المستشفى وكذلك الوفيات. تم استخدام الإحصائيات الوصفية وكذلك الانحدارات اللوجستية المتعددة بفاصل ثقة 95٪ لتحليل البيانات. تم ضبط مستوى الدلالة الإحصائية عند 0.05.

النتائج: بلغ متوسط مدة الإقامة في المستشفى 6 أيام. كانت الأعراض التالية أكثر شيوعا: السعال (63.5٪)، الحمى (50٪)، ضيق التنفس (46.1٪)، وآلام العضلات (40.8٪) على التوالي. كان ارتفاع ضغط الدم (29.5٪) والسكري (24.7٪) وأمراض القلب والأوعية الدموية (21.8٪) أكثر الأمراض المصاحبة انتشاراً على التوالي. وكان معدل وفيات الحالات 8.30٪. تزيد الأعراض التنفسية من احتمالات الوفاة بنسبة 45٪ (نسبة الأرجحية = 1.45، مجال الموثوقية 95٪: 1.03 – 2.06). ارتبطت أعراض الجهاز الهضمي بانخفاض معدل وفيات الحالات، ولكن هذا الارتباط لم يكن ذا دلالة إحصائية (نسبة الأرجحية: 0.94، فاصل الثقة 95٪: 0.73–1.21).

الاستنتاجات: تؤكد نتائج هذه الدراسة ارتفاع معدل الوفيات بين الفئات العمرية الأكبر سنا والمرضى الذكور وحالات كوفيد-19 المصابة بأمراض مصاحبة.

الكلمات المفتاحية: كوفيد-19؛ السمات السريرية؛ معدل وفيات الحالات؛ فيروس سارس-2؛ الحالات المنومة

Abstract

Objective: Identifying the epidemiological characteristics of COVID-19 could help to control the pandemic. The aim of this study was to characterize the epidemiological features of hospitalized COVID-19 patients in Iran.

Methods: Data were collected on patients admitted to a military referral hospital in Tehran, Iran, from February 8, 2020 to July 28, 2021. Sex, age, clinical symptoms, outcome, type of comorbidities, level of blood Spo_2, time of admission, and time of discharge were investigated. Sex ratio, case fatality rate (CFR), and daily trends of hospital admissions and deaths were also determined. Descriptive statistics and multiple logistic regression with 95% confidence intervals were used for data analysis. The statistical significance level was set at 0.05. STATA16.0 and Excel 2010 were used for data analysis.

Results: The median hospital length of stay (LOS) was 6 days. The following symptoms were most common: cough (63.5%), fever (50%), respiratory distress (46.1%), and muscular pain (40.8%). Hypertension (29.5%), diabetes (24.7%), and cardiovascular diseases (21.8%) were the

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Peer review under responsibility of Taibah University.

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most prevalent comorbidities. The CFR was calculated at 8.30%. Respiratory symptoms increased the odds of death by 45% (OR 1.45, 95% CI 1.03−2.06). Gastrointestinal symptoms were associated with a reduction in the mortality of COVID-19 cases, but this association was not statistically significant (OR 0.94, 95% CI 0.73−1.21).

Conclusions: The results of this study emphasize higher mortality rates among older age groups, male patients, and patients with underlying diseases.

Keywords: Case fatality rate; Clinical features; COVID-19; Hospitalized cases; SARS-CoV-2

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Introduction

In 2019, SARS-CoV-2, a highly contagious and novel coronavirus was identified where each infected case infected an average of three other people.[1,2] As of September 26, 2021, 5,519,728 patients with COVID-19 have been identified in Iran, of which 119,082 deaths have been attributed to the virus. According to statistics, Iran ranks eighth in the world in deaths due to COVID-19.[3]

The virus is transmitted through droplets from the nose when coughing and sneezing. Common symptoms of COVID-19 include fever, dry cough, and fatigue.[4] There may be other symptoms such as muscular pain, loss of smell and taste, sore throat, and headache. Shortness of breath and chest pain are among the more serious symptoms of the disease. Vaccination, social distancing, hand hygiene, and face masks are among the common measures to contain the pandemic.[5] The clinical manifestation of the disease is often mild and the disease is usually self-limited. However, COVID-19 is a serious risk to the elderly and to people with underlying diseases such as cardiovascular disease, diabetes, cancer, and chronic lung disease.[6,7]

The epidemiological features of hospitalized COVID-19 patients in Iran have been previously reported.[8] Our study was based on data from February 8, 2020 to July 28, 2021 and aimed to characterize the clinical features, case fatality, and effect of symptoms on mortality among hospitalized cases of COVID-19 in Iran. Here, we report the results of an epidemiological analysis of all cases hospitalized at a military referral hospital in Tehran, Iran.

Materials and Methods

Study design and data collection

This retrospective epidemiological study was performed on hospitalized patients with COVID-19 at a military hospital in Tehran from February 8, 2020 to July 28, 2021. All data were kept confidential. The disease was confirmed by reverse transcription-polymerase chain reaction (RT-PCR) using throat and nose swab specimens from the upper respiratory tract or clinically diagnosed based on lung imaging features (chest computed tomography scan ground glass pathognomonic). The study variables were as follows: sex, age, clinical symptoms, outcome (including death or survival), types of comorbidities, level of blood Spo_2, time of admission, and time of discharge.

Statistical analysis

Descriptive results were expressed as the mean (± standard deviation, SD), median (with an interquartile range, IQR = $Q_1 - Q_3$), or number (%). The missing data were not imputed. The sex ratio (male to female) and the case fatality rate (CFR) were calculated. Odds ratios (ORs) based on multiple logistic regression with 95% confidence intervals (CIs) were calculated. The statistical significance level was set at 0.05. STATA version 16.0 and Excel version 2010 were used for data analysis.

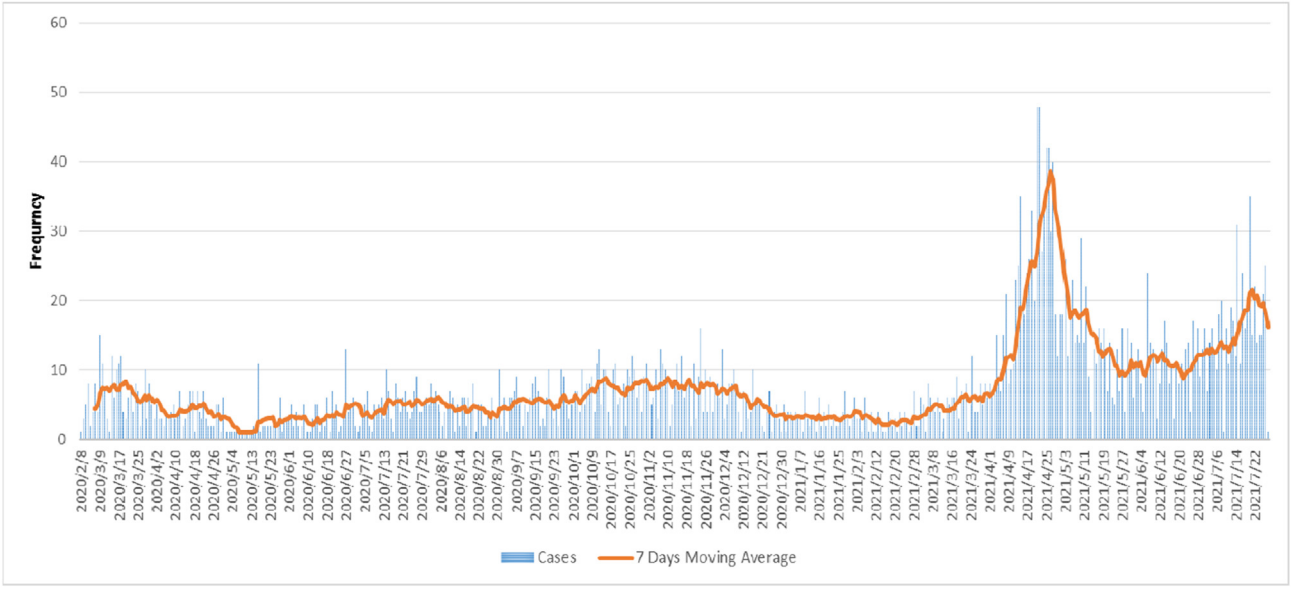

Figure 1: COVID-19 hospital admissions during the study period.

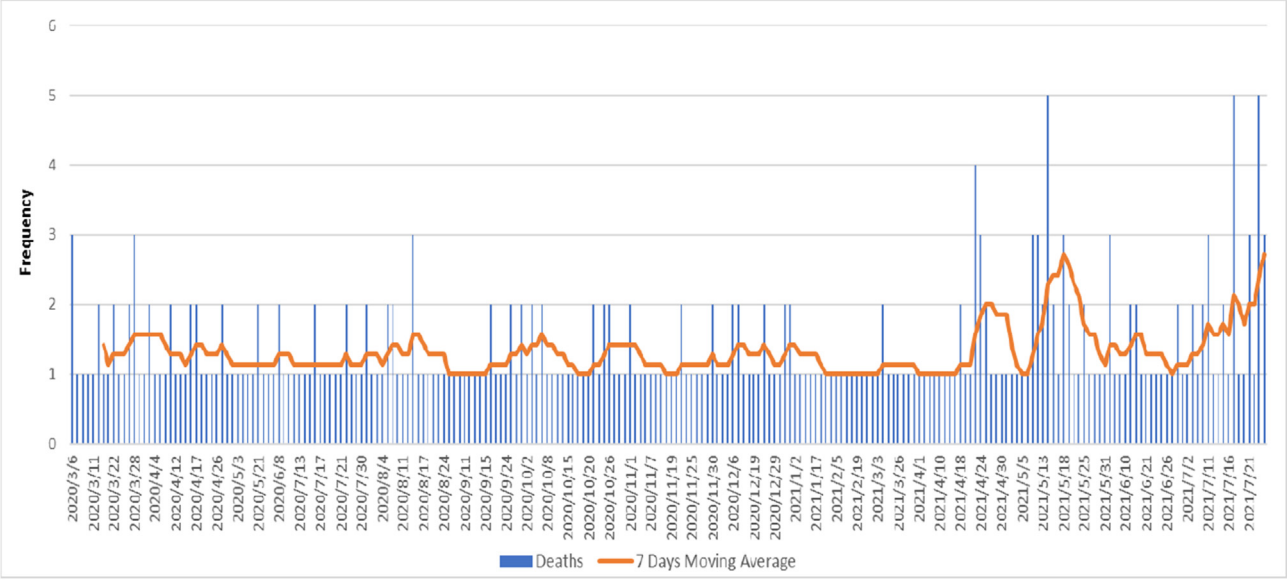

Figure 2: Deaths among hospitalized cases of COVID-19 during the study period.

Results

All of the cases (3759) were approved by chest CT scan, and 1016 (27%) of cases were PCR negative. The mean age of the patients was 57.48 ± 17.27 years, and the median age was 59 (70−45) years. Most of the cases were in the age group of 61−70 years (819, 21.78%). According to hospital records, the hospital readmission rate was about 0.004 or 4 cases per 1000 hospitalized cases. The median (interquartile range) time from discharge to hospital readmission in these cases was 9 (24−3) days.

Also, most cases (2147, 57.1%) were male. The male-to-female ratio was 1.33:1.0. The mean hospital length of stay (LOS) was 7.18 ± 6.22 days and the median LOS was 6 (8−4) days. Figures 1 and 2 depict the trend of hospital admissions and deaths from COVID-19 during the study period. Overall, 556 (14.8%) cases were admitted to the ICU, and 1308 (34.8%) had positive contact history with COVID-19 cases.

More information about the baseline clinical information is shown in Table 1. The most common symptoms in hospitalized cases were cough (63.5%), fever (50%), respiratory distress (46.1%), and muscular pain (40.8%) (Table 2). The most prevalent comorbidities among COVID-19 cases were hypertension (29.5%), diabetes (24.7%), and coronary heart diseases (21.8%) (Table 2).

Table 1: Baseline and clinical characteristics of hospitalized COVID-19 cases.

Variable	*n* (%)
Sex	
Male	2147 (57.1)
Female	1612 (42.9)
Inpatient section	
General section	3203 (85.2)
ICU	556 (14.8)
Positive contact history	1308 (34.8)
Re-admission	17 (0.5)
Intubation	213 (5.7)
$Po_2 < 93$	918 (24.4)
Smoking	150 (4.0)
Drug abuse	65 (1.7)
PCR results	
Negative	1016 (27.0)
Positive	2743 (63.0)
Final status	
Alive	3445 (91.6)
Dead	313 (8.3)
Total	3759 (100.0)

Table 2: Distribution of symptomatology and comorbidities among hospitalized COVID-19 cases.

Symptom	*n* (%)	Comorbidity	*n* (%)
Cough	2385 (63.5)	Hypertension	1109 (29.5)
Fever	1878 (50.0)	Diabetes	931 (24.7)
Respiratory distress	1733 (46.1)	Cardiovascular	820 (21.8)
Muscular pain	1532 (40.8)	Other chronic disorders	487 (12.9)
Anorexia	1369 (36.4)	Blood disorders	16 (0.4)
Headache	954 (25.4)	Kidney diseases	90 (2.4)
Nausea	822 (21.9)	Asthma	119 (3.1)
Chest pain	489 (13)	Cancer	74 (1.9)
Dizziness	476 (12.7)	Liver diseases	47 (1.2)
Diarrhea	392 (10.4)	Immune deficiency	6 (0.1)
Loss of smell	362 (9.6)	Chronic obstructive pulmonary disease	32 (0.8)
Abdominal pain	329 (8.8)	Neurological disorders	32 (0.8)
Vomit	314 (8.4)		
Loss of taste	251 (6.7)		
Loss of consciousness	129 (3.5)		
Convulsion	19 (0.5)		
Skin lesion	8 (0.2)		

Table 3: Distribution of cases, deaths, and case fatality rate among hospitalized COVID-19 cases.

Variable	Subgroup	All cases	Deaths, *n* (%)	Case fatality rate, %
Overall		3759	313	8.30
Age group (years)	0–10	15	0 (0.0)	0.00
	11–20	47	2 (0.63)	4.26
	21–30	175	1 (0.31)	0.57
	31–40	441	9 (2.87)	2.04
	41–50	595	19 (6.07)	3.19
	51–60	754	28 (8.94)	3.71
	61–70	819	77 (24.60)	9.40
	71–80	552	85 (27.15)	15.40
	>80	360	92 (29.39)	25.56
Sex	Female	1612	114 (36.42)	7.07
	Male	2146	199 (63.57)	9.27
Smoking status	No	3609	301 (96.16)	8.34
	Yes	150	12 (3.83)	8.00
Drug addiction	No	3695	299 (95.52)	8.09
	Yes	64	14 (4.48)	21.88
Symptoms	Gastrointestinal	1981	149 (47.60)	7.52
	Respiratory	3138	270 (86.26)	8.60
	Other symptoms	2821	180 (57.50)	6.38
Comorbidity	Cancer	74	16 (5.11)	21.62
	Diabetes	931	106 (33.86)	11.39
	Cardiovascular diseases	820	127 (40.57)	15.49
	Kidney diseases	90	21 (6.70)	23.33
	Asthma	119	8 (2.56)	6.72
	Hypertension	1109	129 (41.21)	11.63
Po_2	<93	918	65 (20.76)	7.08
	≥93	2841	248 (79.23)	8.73
Ward	General	3203	21 (6.70)	0.66
	ICU	555	292 (93.29)	52.61
PCR results	Negative	1016	95 (30.35)	9.35
	Positive	2743	218 (69.65)	7.95

Table 4: Odds ratios (ORs) for mortality according to different symptoms subgroups.

Variable	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
Outcome = death (n = 3758, event = 313)			
Without symptoms	Reference	Reference	Reference
Gastrointestinal symptoms	0.80 (0.63–1.02)	0.93 (0.72–1.19)	0.94 (0.73–1.21)
Respiratory symptoms	1.18 (0.84–1.65)	1.48 (1.05–2.10)	**1.45 (1.03–2.06)**
Other symptoms	**0.42 (0.33–0.53)**	0.56 (0.44–0.73)	**0.57 (0.44–0.73)**

Model 1: Crude model.
Model 2: Model 1 + age, sex.
Model 3: Model 2 + cancer, hypertension, coronary heart diseases, chronic liver diseases, diabetes, asthma, chronic lung diseases.
Significant values are in bold.
Other symptoms: fever, headache, muscular pain, loss of taste, convulsions, dizziness.

During the study period, 313 deaths occurred, so the overall CFR among hospitalized cases was 8.30%. Patients over 80 years of age had the highest CFR among the age groups (25.56%). The CFR for men and women was 9.27% and 7.07%, respectively. According to comorbidity conditions, higher CFRs were seen in COVID-19 patients with kidney diseases (23.33%), cancer (21.62%), and cardiovascular diseases (15.49%). The CFR among patients who were admitted to the general section and to the ICU was 0.66% and 52.61%, respectively. According to symptoms, the CFR among cases gastrointestinal, respiratory, and other symptoms (fever, headache, dizziness, etc.) was 7.52%, 8.60%, and 6.38%, respectively (Table 3).

The results of multiple logistic regression showed that respiratory symptoms significantly increased the odds of death by 45% (OR 1.45, 95% CI 1.03–2.06). Also, gastrointestinal symptoms were associated with a reduction in mortality of COVID-19 cases but this association was not statistically significant (OR 0.94, 95% CI 0.73–1.21). Having other symptoms (fever, headache, dizziness, etc.) was significantly associated with a reduction in mortality of COVID-19 cases (OR 0.57, 95% CI 0.44–0.73) (Table 4).

Discussion

The present study aimed to describe the epidemiology, clinical features, case fatality, and effect of symptoms on mortality and hospitalized cases. In this study, the CFR of COVID-19 was higher in men than women and the highest CFR was in people over 80 years (25.25%). A meta-analysis by Biswas et al. showed that male sex and age above 50 years were associated with an increased risk of mortality.[9] Many studies have shown higher mortality in males compared to females.[10–12] One explanation may be related to the role of genes. The angiotensin-converting enzyme (ACE2) gene plays a key role in the virus entering the cell, which is located on the X chromosome and can play a different role in women who are heterozygous than in homozygous men.[13] Other studies showed a higher CFR among older patients, and age has been suggested as a risk factor for death among ICU patients.[14,15] According to the Korea Center for Disease Control and Prevention, 10.9% of deaths were observed in people aged 70–79 years and 26.6% were in people over 80 years old.[11] In Italy, the highest CFR was observed in people aged 70–79 years and over 80 years old (16.9% and 24.4%, respectively).[12] In fact, the severity of the disease and the higher CFR at older ages may not be directly related to age but rather due to the greater prevalence of chronic diseases in these people, who subsequently have weaker immune systems.[16,17]

In the present study, the mean age of patients was 57 years and most of the cases were seen in the age group of 60–70 years. This may indicate a lower risk of hospitalization among young people, which is consistent with other studies.[8,18] In this study, cough and fever were the most common symptoms in hospitalized patients. In the study of Moon et al., the mean age of patients was 56 years. Cough and fever were the most common symptoms among hospitalized patients.[19] In a study by Lee et al., in South Korea, no severe cases of the disease were observed in people under 19 years of age, and cough was the most common symptom among hospitalized patients (59%).[20] Old age has also been reported as one of the risk factors of severe acute respiratory syndrome (SARS) which, as mentioned above, could be due to the high prevalence of chronic diseases in these patients.[21] The CFR is estimated at approximately 2% among cases of SARS-CoV-2 worldwide. This index varies from 0.9% in Turkey to 18.7% in Yemen, and it is 2.2% in Iran.[22] The CFR is higher in hospitalized patients compared to the general population. Our study showed that the CFR in hospitalized patients was 8.5%, about four times that of the general population. The CFR in hospitalized patients may depend on several factors, such as the virulence of SARS-CoV-2, population vulnerability (age and sex), the quality of the healthcare system, the definition of morbidity and mortality, and the accuracy of data recording. Thus, it is perhaps illogical to compare this index among different countries or locations.[23]

In the present study, the admission of patients to the ICU was 14.8% and ICU patients had the highest CFR (52.6%). In a meta-analysis study by Zhang et al., ICU admission was 10.9%,[24] similar to our results. In other studies, ICU admission has been reported to be about 10%.[25] Some biochemical factors such as leukocyte count, alanine aminotransferase, aspartate transaminase, high lactate dehydrogenase (LDH), and elevated procalcitonin had been reported to be associated with increased ICU admission and patient mortality.

Re-infection with COVID-19 could be due to several reasons: time has passed for the virus-neutralizing antibody, the type of sample collection and technical errors associated with the test, methods used before discharge, and the presence of viral RNA in the stool.[26] In our study, the proportion of hospital re-admission was 0.5%. This low rate may indicate temporary protection against the virus after infection. Due to the possibility of mutation in the virus, however, it is necessary to apply protective and preventive functions during and after recovery.

Comorbidity due to decreased immune system function and polypharmacy can cause severe disease.[27] In the present study, the highest CFR was in renal (23%), cancer (21.6%), heart disease (15.49%), hypertension (11.63%), and diabetes (11.39%) patients. In a meta-analysis study, kidney disease ranked first and cardiovascular diseases ranked third in mortality.[14] The association between higher mortality and comorbidities has also been reported in other studies.[28,29] SARS-CoV-2 virus enters cells via the ACE2 receptor, an enzyme found in the heart, lungs, brain, and kidneys in abundance. This is probably the reason for the increased severity of SARS-CoV-2 in kidney, heart, and lung patients.[30,31]

On the other hand, this study showed the highest CFR in people who had respiratory symptoms and other symptoms such as fever and headache. We found that respiratory symptoms increased the odds of mortality by 45%. In a meta-analysis study performed on cohort studies comparing two groups—patients admitted to the ICU and patients not admitted to the ICU—among the symptoms, fever and shortness of breath showed a significant relationship with the severity of the disease and admission to the ICU, and patients admitted to the ICU had higher mortality rates and lower discharge rates.[32]

The present study had a relatively large sample size (3759). However, one of the limitations of the study pertains to hospital data. The data in the current study had not been collected for research purposes and were often incomplete or illegible. Moreover, para-clinical variables and treatment procedures are among the main factors predicting the severity of the disease,[24] and these were not considered in our study.

Conclusions

The results of this study emphasize the higher mortality rate among older age groups, male patients, and patients with underlying diseases. Our results further indicate the importance of paying attention to the symptoms (especially respiratory symptoms) of patients upon arrival at the hospital. As SARS-CoV-2 continues to mutate, the pathogenicity and other epidemiological indicators of the disease can change, and this warrants close investigation.

Source of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sector.

Conflict of interest

The authors have no conflict of interest to declare.

Ethical approval

This study was approved by the ethical committee of AJA University of Medical Sciences.

(IR.AJAUMS.REC.1399.065). Data records were anonymous, so informed consent was waived.

Authors contributions

YA and MS conducted the search, data analysis, and manuscript preparation. RR, HSN, and SA helped prepare the manuscript and its English edition. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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How to cite this article: Alimohamadi Y, Sepandi M, Rashti R, Sedighinezhad H, Afrashteh S. COVID-19: Clinical features, case fatality, and the effect of symptoms on mortality in hospitalized cases in Iran. J Taibah Univ Med Sc 2022;17(5):725–731.