Global Epidemiology 3 (2021) 100046

Contents lists available at ScienceDirect

Global Epidemiology

journal homepage: https://www.journals.elsevier.com/global-epidemiology

Risk factors of developing critical conditions in Iranian patients with COVID- 19

Alireza Arman [a,1], Maryam Tajik [b,1], Maryam Nazemipour [c], Zahra Ahmadinejad [d], Sahar Keyvanloo Shahrestanaki [e], Ebrahim Hazrati [f], Nasrin Mansournia [g], Mohammad Ali Mansournia [h,*]

[a] Medical-Surgical Department School of Nursing & Midwifery Tehran University of Medical Sciences, Tehran, Iran
[b] Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[c] Psychosocial Health Research Institute, Iran University of Medical Sciences, Tehran, Iran
[d] Liver Transplantation Research Center, Department of Infectious Diseases, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran
[e] Nursing Care Research Center(NCRC), School of Nursing and Midwifery, Iran University of Medical Science, Tehran, Iran
[f] Department of Anesthesiology, AJA University of Medical Sciences, Tehran, Iran
[g] Department of Endocrinology, AJA University of Medical Sciences, Tehran, Iran
[h] Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

ARTICLE INFO

Article history:
Received 13 November 2020
Received in revised form 4 December 2020
Accepted 4 December 2020
Available online 08 December 2020

Keywords:
COVID-19
Coronavirus
Mortality
Management

ABSTRACT

COVID-19 due to novel Coronavirus was first reported in Wuhan, China. Nowadays, the Islamic Republic of Iran stands among countries with high COVID-19 prevalence and high burden of disease. Since the medical resources are limited, we aimed to identify the risk factors for patients developing critical conditions. This can help to improve resource management and treatment outcomes. In this retrospective study, we included 12,677 patients who were from 26 hospitals, supervised by Tehran University of Medical Sciences with signs and symptoms of COVID-19, until April 12. University integrated IT system was adopted to collect the data. We performed Logistic regression to evaluate the association between death in COVID-19 positive patients and other variables. Cough, respiratory distress and fever were the most common symptoms in our patients, respectively. Cancer, chronic lung diseases and chronic neurologic diseases were the strongest risk factors for death in COVID-19 patients.

Introduction

Coronaviruses are a group of RNA-coated viruses that cause widespread respiratory, intestinal, liver, and neurological diseases in humans and other mammals and birds [1]. Until a few months ago, six species of Coronavirus were known as human pathogens. These include E 229, OC43, NL63, and HKU1 viruses, which are very common and typically cause cold symptoms in immunodeficient people [2]. The other two types of Coronaviruses are acute respiratory syndrome (SARS-CoV) and Middle East Respiratory Syndrome (MERS-COV), which are zoonotic in origin and are sometimes fatal [3].

In December 2019, a novel Coronavirus (COVID-19, SARS-CoV-2) with zoonotic nature was reported in Wuhan, China [4,5]. Numerous human factors including poor assessment of the possible risks of the virus, the location of Wuhan city, the vastness of the communication network of the people of this city and Chinese New Year, in addition to the virus's characteristics, including its high rate of transmission through human-to-human contact through droplets and the incubation period, caused the virus to spread rapidly from Wuhan all over China and from China to other parts of the world [6–8].

Soon, on January 2020, the first case out of China was confirmed in Thailand. By the end of January 2020, a rapid increase of cluster cases happened around the world and WHO declared that this epidemic was a public health emergency of international concern (PHEIC) [9]. In Iran, the Ministry of Health announced positive results for corona tests in two patients on February 19, 2020. Nowadays, COVID-19 is rapidly spreading and fighting with it is a global challenge. There have been more than 58 million confirmed cases of COVID-19 and more than 1,390,300 deaths, reported as of 18 November 2020 [10]. Since the pathogen is new, our knowledge about the disease and its epidemiological parameters is incomplete.

COVID-19 can affect anyone regardless of age, gender and race [11]. Despite the fact that anyone who has had close contact with infected patients is susceptible to novel coronavirus, it is not predictable whether they will become infected or not [12,13]. People can transfer the disease before they become symptomatic and about 44% of the transmission occurs in this period [14,15].

This disease can present with different symptoms from fever, cough, shortness of breath, myalgia, diarrhea, loss of smell, taste and loss of

* Corresponding author at: Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, PO Box: 14155-6446, Tehran, Iran.
E-mail address: mansournia_ma@sina.tums.ac.ir (M.A. Mansournia).
[1] Joint first author.

https://doi.org/10.1016/j.gloepi.2020.100046

consciousness, and headache [9]. Symptoms usually resolve after ten days in 90% of cases and after 15 days nearly all cases but viral shedding continues for about 18 days [16–19]. Severe cases have 60 times more viral load than mild cases and they may continue shedding the virus for even 25 days [20]. However, some people do not develop symptoms but can transfer the disease [21–23]. Younger people are more likely to remain asymptomatic [21]. Older people and those with immunodeficiency are more likely to develop severe illness [12,24]. Infection in severe cases may lead to pneumonia, organ failure and death [12].

Th increasing number of people with COVID-19 has increased the need for beds in intensive care units (ICUs) [25]. So far, very little research has been done on the risk factors for hospitalization in ICU wards and the mortality of patients with novel coronavirus. Some researchers have indicated that male gender, age and comorbidities such as ischemic heart disease, diabetes and hypertension increases are risk factors of mortality in COVID-19 patients [26]. However, risk factors of developing critical conditions in these patients is still a controversial issue.

Iran has had more than 866,000 confirmed cases and near 45,255 deaths until 18 November 2020 [10]. The number of cases is growing and medical resources are limited [27]. Therefore, identifying the patients at higher risk for critical conditions helps to manage the disaster. In this study, we described the characteristics of COVID-19 patients and also assessed the risk factors for mortality in the hospitals of Tehran University of Medical Sciences, Tehran, Iran.

Methods

In this study, we evaluated the information of 12,677 patients who had been referred to the hospitals affiliated to Tehran University of Medical Sciences, Tehran, Iran with COVID-19 symptoms from January 21 to April 12, 2020. The hospitals have been listed in the supplementary Table S1. We did not have any exclusion criteria in this study.

Data were obtained using the university's integrated MCMC (medical care monitoring center) system. We recorded age, gender, underlying medical conditions (including hypertension, diabetes mellitus, immunodeficiencies, heart disease, pulmonary disease, etc.), history of close contact with infected people, COVID-19 symptoms (including fever, cough, dyspnea, myalgia etc.), smoking, drug addiction, chest CT scan reports and real-time reverse transcriptase polymerase chain reaction (RT-PCR) results. Due to low and variable sensitivity of RT-PCR (40–70%) we enrolled all patients with possible (typical signs and symptoms for COVID-19 infection), probable (typical coronavirus signs and symptoms with typical radiological findings) and definite (suspicious signs and symptoms and positive RT-PCR test from respiratory secretions) diagnosis of COVID-19 infection. The diagnostic test used in Iran was the PCR for respiratory tract secretions which were sent to the virology section at School of Public Health, TUMS (which is one of the reference virology labs in Iran). The results were sent to the hospital every other day. PCR was taken from people who had 3 of the following symptoms: fever, coughing, muscular pain and headache.

Since this was a retrograde study with minimal risk and we used routine data collected from the patients, informed consent was not obtained from the patients. This study was submitted and confirmed by the ethics committee of Tehran University of Medical Sciences with the ethical code of IR.TUMS.VCR.REC.1399.013.

Statistical analysis

We used Stata version 14.2 for statistical analysis. Descriptive statistics were presented by mean and standard deviation (SD) for continuous variables, and frequencies and percentages for categorical variables. Logistic regression was performed to evaluate the association between death and other variables.

Results

We enrolled 12,677 people including 5742 (45.29%) females from 26 hospitals, Tehran, Iran. Fourteen hospitals were educational and affiliated with Tehran University of Medical Sciences (TUMS) and the others were private, charity or belonged to other organs but supervised by TUMS during the COVID-19 pandemic. The mean (SD) age of the participants was 50.01 (17.72). There were 60 pregnant (1.4%) women in this population. Contact with COVID-19 positive patients were reported from 1922 (15.16%) of the patients. Samples from 5895 (46.26%) patients were sent for RT-PCR. Among these, 2100 (35.62%) of the samples were positive for COVID-19, 2413 (40.93%) were negative and 1382 (23.44%) of the test results were not ready till the end of the study. Chest CT scan was performed for 854 patients and 683 (79.97%) of them were compatible with COVID-19 patterns. Peripheral capillary oxygen saturation (SpO2) of the patients was evaluated at the time of admission and 4055 (31.99%) of them had SpO2 less than 93%.

Among the included patients, 10,684 (84.31%) were admitted to general wards, 104 (0.82%) were isolated and 1885 (14.87%) were admitted to intensive care units (ICUs). During the hospitalization period 437 (3.45%) patients were intubated.

Table 1 summarizes patients' coexisting medical conditions. The most frequent underlying diseases were heart disease and diabetes mellitus with 948 (7.48%) and 855 (6.74%) patients, respectively.

Patients presented with different signs and symptoms. Table 2 shows the detailed information about patients' symptoms at the time of admission. The most common symptoms were cough (47.39%), respiratory distress (34.42%) and fever (34.26%).

Frequency of smoking and drug abuse among our patients were 78 (1.46%) and 25 (0.47%), respectively.

During the study, we recorded 843 (6.65% of total population) deaths that included 407 patients in general wards, one patient in isolated room and 431 patients (3.40%) in ICUs. There were 322 (38.19%) female and 521 (61.80%) male patients among deaths. Death rate among intubated patients was 58.12% (254 patients). Mortality of test positive patients was 376 (17.90%).

Logistic regression revealed that cancer (OR = 4.31, 95% CI: 2.29–8.11), chronic lung diseases (OR = 3.39, 95% CI: 1.64–6.98) and chronic neurologic diseases (OR = 3.30, 95% CI: 1.04–10.47) are the strongest risk factors for death in COVID-19 patients (Table 3). Table 3 shows underlying conditions that are associated with death in COVID-19 patients. Complete results have been presented in the supplementary Table S2.

Patients who were intubated had the highest odds for death (OR = 13.96, 95% CI: 9.36–20.81). Loss of consciousness (OR = 8.34, 95% CI: 4.67–14.89) and respiratory distress (OR = 1.48, 95% CI: 1.18–1.86)

Table 1
The underlying diseases in all patients and COVID-19 positive patients.

Underlying diseases	All patients (n = 12,677)		COVID-19 positive patients (n = 2100)	
	Frequency	Percentage	Frequency	Percentage
Diabetes Mellitus	855	6.74	236	11.24
Heart Disease	948	7.48	267	12.71
Hypertension	226	4.24	32	3.90
Chronic Kidney Disease	187	1.48	51	2.43
Asthma	161	1.27	24	1.14
Other Chronic Lung Diseases	166	1.31	31	1.48
Chronic Blood Disease	82	0.65	23	1.10
Chronic Liver Disease	55	0.43	10	0.48
Chronic Neurologic Diseases	50	0.39	12	0.57
Other Chronic Diseases	556	4.39	130	6.19
Cancer	204	1.61	40	1.90
HIV-AIDS	17	0.13	1	0.05
Immunodeficiency	43	0.34	7	0.33

Table 2
Symptoms and signs in all and COVID-19 patients.

Symptoms and signs	All patients ($n = 12,677$)		COVID-19 positive patients ($n = 2100$)	
	Frequency	Percentage	Frequency	Percentage
Cough	6008	47.39	1024	48.76
Respiratory Distress	4363	34.42	765	36.43
Fever	4343	34.26	932	44.38
Muscular Pain	3644	28.74	582	27.71
Loss of Consciousness	240	1.89	51	2.43
Loss of Smell	130	2.44	10	1.22
Loss of Taste	14	0.11	2	0.10

also increased the risk of death. The results of logistic regression of mortality on patients' signs and symptoms have been presented in the supplementary Table S3.

Discussion

Historically, one of the global challenges has always been emerging pathogens. One of these challenges is Coronavirus [25,28]. In December 2019, the new Coronavirus has been introduced as the seventh member of the coronavirus family, which is different from both MERS-CoV and SARS-CoV and infects humans [3]. Iran is currently fifteenth in terms of statistics and the number of deaths in the world (until 18 Nov 2020) [10]. Due to growing number of the cases and limited medical resources, early identification of the patients at higher risk for critical conditions is necessary for delivering proper treatment and optimizing the use of resources [27,29,30].

Based on a review published in June 2020, most common symptoms are reported to be fever and cough [13]. A recent study from Iran, represents cough, fever and respiratory distress as the most prevalent symptoms [31]. These are consistent with our study as cough, respiratory distress and fever were reported more than other symptoms. Nowadays the symptoms are divided into four types that represent the severity level (mild, moderate, severe, critical) of the disease [32]. Fever may be presented in all four types of the disease. However, respiratory symptoms and oxygen saturation are key indicators for differentiation of the severity level [32].

Hypertension, diabetes mellitus and cardiovascular disease were most common comorbidities, in previous studies [13,31]. Some comorbidities including hypertension, cardiovascular disease, chronic kidney disease and cerebrovascular disease are associated with severity of the disease [13]. Interestingly, the rate of HIV/AIDS as comorbidity was very low in our study. A similar result has reported from another study which evaluated the prevalence of COVID-19 signs and symptoms among outpatient people who lived with HIV (PLWH) [32]. Among 200 PLWH, only one had confirmed diagnosis of COVID-19 infection [33]. This is possible that PLWH, especially whom receive antiretroviral agents may be less susceptible to COVID-19 infection at least in sever form of disease.

Case-fatality rate (CFR) is the total number of deaths divided by the total number of infected patients. CFR depends on different factors. WHO estimated global CFR to be 3.8% [33]. CFR has a direct relation with age and is higher in older patients [13]. In a report of 72,314 patients, overall case-fatality rate (CFR) was reported 2.3% but it was higher in patients with cardiovascular disease, more than 70 years old, diabetes, chronic lung disease, hypertension and cancer [34]. A retrospective cohort of Iranian patients showed 24.4% in-hospital mortality rate in 30 days [31]. In our study, mortality rate of COVID-19 patients was 17.9% and about half of these patients were in intensive care units.

Table 3
Selecting underlying conditions associated with death in COVID-19 patients.

Variable	Odds ratio	95% Confidence interval
Cancer	4.31	2.29–8.11
Chronic lung diseases	3.39	1.64–6.98
Chronic neurologic diseases	3.30	1.04–10.47
ICU admission	2.28	2.02–2.58
Age (10 years)	1.72	1.58–1.86
Heart disease	1.65	1.22–2.23
Gender	1.46	1.16–1.84

A retrospective cohort study introduced a clinical risk score for COVID-19 patients that evaluates the risk of developing critical conditions including invasive ventilation, ICU admission and death [35]. Age, dyspnea, unconsciousness, cancer history, hemoptysis, direct bilirubin, neutrophil to lymphocyte ratio, lactate dehydrogenase, number of comorbidities (Chronic obstructive pulmonary disease, diabetes, hypertension, coronary heart disease, chronic kidney disease, immunodeficiency, cancer, cerebral vascular disease and hepatitis B) and chest radiography abnormality, were included in this risk score. Our study showed that cancer, chronic lung diseases, chronic neurologic diseases, ICU admission, age (every 10 years), heart disease and male gender increase the mortality rate in COVID-19 Patients.

Malignancies are known as mortality risk factor of lots of diseases including COVID-19 [13,35,36]. Prevalence of COVID-19 may be lower in patients with history of cancer [37]. The exact reason is unknown. However, cancer has an independent association with higher mortality of these patients [37]. In this study, cancer had the highest odds ratio among all other risk factors. Respiratory problems, especially chronic lung disease worsen the patients' condition and increase mortality [36,38]. A recent study showed that longer history of COPD results in more negative outcomes and more death rate [38].

Literature has revealed that novel coronavirus in patients with pre-existing neurological diseases is associated with poor outcomes [39,40]. A study in Spain indicated that chronic neurologic disease is among the most relevant comorbidities of COVID-19 [37].

Almost all of the researches showed that there is a relation between age and developing critical condition in COVID-19 patients. The need for intensive care unit (ICU) admission is higher in older patients [41]. Many researchers indicated that patients older than 60–65 years old are at higher risk of mortality [13,36]. In a recent study, most of the deaths were of patients with 70 to 89 years old [37]. In our study, there was an increase in death rate with age.

Pre-existing cardiovascular problems especially coronary heart disease put the patient at great risk of developing fatal form of novel coronavirus disease [41]. Lots of studies have mentioned cardiovascular diseases especially ischemic heart disease as a risk factor for mortality in COVID-19 patients [13,26,36]. However, there are some studies that did not find relation between cardiovascular diseases and mortality rate [37].

Evidence suggests that mortality rate of novel coronavirus is higher in men [36]. Meta-analysis studies showed that male gender is a risk factor for disease progression and has an association with mortality [42,43].

Limitations

This study had some limitations. First, we collected data from one province. However, because Tehran is capital, we had patients from all over the country. Second, RT-PCR assay was not performed for all of the patients. Third, we did not include laboratory variables and did not perform multivariable logistic regression analysis as the laboratory data were not available at the time of this study. Forth, some signs and symptoms that recently were recognized as presentation for COVID-19 (including diarrhea) were not included in our database. Fifth, some inflated OR estimates and confidence limits in our results suggest the possibility of sparse-data bias [44,45]. In fact, we could not assess the association between some uncommon variables such as HIV, drug abuse,

immune deficiency, and loss of taste or smell with death due to an extreme formal sparse-data bias known as separation [46].

Conclusion

This is one of the first studies that describes the risk factors of death in novel coronavirus patients in Iran. We found higher mortality in patients with male gender, older age, cancer, heart disease, chronic lung disease and chronic neurological disease.

Declaration of Competing Interest

Mohammad Ali Mansournia is a Senior Associate Editor on Global Epidemiology. Authors declare no conflict of interests in performing this research.

Acknowledgement

Authors would like to appreciate the support and constructive comments of the methodologist research development office, Imamkhomeini Hospital complex, Tehran, Iran. This research has been supported by Tehran University of Medical Sciences & health services grant 99-1-99-47243. We would also like to acknowledge the cooperation of Vice Chancellor for Treatment and IT unit of Tehran University of Medical Sciences. We thank all the doctors, nurses and people involved in the diagnosis, treatment and care of COVID-19 patients.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.gloepi.2020.100046.

References

[1] Wu F, Zhao S, Yu B, et al. A new coronavirus associated with human respiratory disease in China. Nature. 2020;579:265–9.
[2] Su S, Wong G, Shi W, et al. Epidemiology, genetic recombination, and pathogenesis of coronaviruses. Trends Microbiol. 2016;24:490–502.
[3] Ahmad T, Khan M, Haroon, et al. COVID-19: Zoonotic aspects. Travel Med Infect Dis. 2020;36:101607.
[4] Li Q, Guan X, Wu P, et al. Early transmission dynamics in Wuhan, China, of Novel coronavirus-infected pneumonia. N Engl J Med. 2020;382:1199–207.
[5] Wang C, Horby PW, Hayden FG, Gao GF. A novel coronavirus outbreak of global health concern. Lancet. 2020;395:470–3.
[6] Peeri NC, Shrestha N, Rahman MS, et al. The SARS, MERS and novel coronavirus (COVID-19) epidemics, the newest and biggest global health threats: what lessons have we learned? Int J Epidemiol. 2020;49:717–26.
[7] Lai C-C, Shih T-P, Ko W-C, Tang H-J, Hsueh P-R. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and corona virus disease-2019 (COVID-19): the epidemic and the challenges. Int J Antimicrob Agents. 2020;105924.
[8] Del Rio C, Malani PN. COVID-19-new insights on a rapidly changing epidemic. Jama. 2020;323:1339–40.
[9] Sun J, He WT, Wang L, et al. COVID-19: epidemiology, evolution, and cross-disciplinary perspectives. Trends Mol Med. 2020;26:483–95.
[10] World Health Organization. WHO Coronavirus Disease (COVID-19) Dashboard. Available from: https://covid19.who.int/; 2020.
[11] Guan W-J, Ni Z-Y, Hu Y, et al. Clinical characteristics of 2019 novel coronavirus infection in China MedRxiv ; 2020.
[12] Park M, Cook AR, Lim JT, Sun Y, Dickens BL. A systematic review of COVID-19 epidemiology based on current evidence. J Clin Med. 2020;9:4.
[13] Siordia Jr JA. Epidemiology and clinical features of COVID-19: a review of current literature. J Clin Virol. 2020;127:104357.
[14] Tindale L, Coombe M, Stockdale JE, et al. Transmission interval estimates suggest pre-symptomatic spread of COVID-19 MedRxiv ; 2020.
[15] He X, Lau EHY, Wu P, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. Nat Med. 2020;26:672–5.
[16] Wang L, Gao YH, Lou LL, Zhang GJ. The clinical dynamics of 18 cases of COVID-19 outside of Wuhan. China Eur Respir J. 2020;55.
[17] Lo IL, Lio CF, Cheong HH, et al. Evaluation of SARS-CoV-2 RNA shedding in clinical specimens and clinical characteristics of 10 patients with COVID-19 in Macau. Int J Biol Sci. 2020;16:1698–707.
[18] Liu Y, Ning Z, Chen Y, et al. Aerodynamic characteristics and RNA concentration of SARS-CoV-2 aerosol in Wuhan hospitals during COVID-19 outbreak BioRxiv ; 2020.
[19] Bai Y, Yao L, Wei T, et al. Presumed asymptomatic carrier transmission of COVID-19. Jama. 2020;323:1406–7.
[20] Liu Y, Yan LM, Wan L, et al. Viral dynamics in mild and severe cases of COVID-19. Lancet Infect Dis. 2020;20:656–7.
[21] Ng OT, Marimuthu K, Chia PY, et al. SARS-CoV-2 infection among travelers returning from Wuhan. China N Engl J Med. 2020;382:1476–8.
[22] Mizumoto K, Kagaya K, Zarebski A, Chowell G. Estimating the asymptomatic proportion of coronavirus disease 2019 (COVID-19) cases on board the diamond princess cruise ship, Yokohama, Japan, 2020. Euro Surveill. 2020;25:2000180.
[23] Rothe C, Schunk M, Sothmann P, et al. Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. N Engl J Med. 2020;382:970–1.
[24] Novel CPERE. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China. Zhonghua liu xing bing xue za zhi= Zhonghua liuxingbingxue zazhi. 2020;41:145.
[25] Zhu N, Zhang D, Wang W, et al. A Novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med. 2020;382:727–33.
[26] Wendel Garcia PD, Fumeaux T, Guerci P, et al. Prognostic factors associated with mortality risk and disease progression in 639 critically ill patients with COVID-19 in Europe: initial report of the international RISC-19-ICU prospective observational cohort. EClinicalMedicine. 2020;25:100449.
[27] Doosti-Irani A, Mostafavi E, Nazemipour M, Mansournia MA, Haghdoost A-A. Challenges for management of the COVID-19 epidemic in Iran. Global Epidemiol. 2020; 100035.
[28] Gao GF. From "A"IV to "Z"IKV: attacks from emerging and re-emerging pathogens. Cell. 2018;172:1157–9.
[29] Shakiba M, Nazemipour M, Heidarzadeh A, Mansournia M. Prevalence of asymptomatic COVID-19 infection using a seroepidemiological survey. Epidemiol Infect. 2020: 1–7.
[30] Shakiba M, Nazemipour M, Salari A, et al. Seroprevalence of SARS-CoV-2 in Guilan Province, Iran. MedRxiv. April 2020;2020.
[31] Jalili M, Payandemehr P, Saghaei A, Sari HN, Safikhani H, Kolivand P. Characteristics and mortality of hospitalized patients with COVID-19 in Iran: a National Retrospective Cohort Study. Ann Intern Med. 2020:M20–2911.
[32] Mazinani M, Rude BJ. The novel zoonotic coronavirus disease 2019 (COVID-19) pandemic: Health perspective on the outbreak. J Healthc Qual Res. 2020.
[33] SeyedAlinaghi S, Ghadimi M, Hajiabdolbaghi M, et al. Prevalence of COVID-19-like symptoms among people living with HIV, and using antiretroviral therapy for prevention and treatment. Curr HIV Res. 2020;18:373–80.
[34] WHO. Coronavirus disease (COVID-2019) situation reports; 2020.
[35] Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA. 2020;323: 1239–42.
[36] Liang W, Liang H, Ou L, et al. Development and validation of a clinical risk score to predict the occurrence of critical illness in hospitalized patients with COVID-19. JAMA Intern Med. 2020;180:1081–9.
[37] Jan H, Faisal S, Khan A, et al. COVID-19: review of epidemiology and potential treatments against 2019 Novel coronavirus. Discoveries (Craiova). 2020;8:e108.
[38] Iftimie S, López-Azcona AF, Vicente-Miralles M, et al. Risk factors associated with mortality in hospitalized patients with SARS-CoV-2 infection. A prospective, longitudinal, unicenter study in Reus, Spain. PLoS One. 2020;15:e0234452.
[39] He Y, Xie M, Zhao J, Liu X. Clinical characteristics and outcomes of patients with severe COVID-19 and chronic obstructive pulmonary disease (COPD). Med Sci Monit. 2020;26:e927212.
[40] Patel U, Malik P, Shah D, Patel A, Dhamoon M, Jani V. Pre-existing cerebrovascular disease and poor outcomes of COVID-19 hospitalized patients: a meta-analysis. J Neurol. 2020:1–8.
[41] Flaherty GT, Hession P, Liew CH, et al. COVID-19 in adult patients with pre-existing chronic cardiac, respiratory and metabolic disease: a critical literature review with clinical recommendations. Trop Dis Travel Med Vaccines. 2020;6:16.
[42] Zheng Z, Peng F, Xu B, et al. Risk factors of critical & mortal COVID-19 cases: a systematic literature review and meta-analysis. J Infect. 2020;81:e16–25.
[43] Patel U, Malik P, Usman MS, et al. Age-adjusted risk factors associated with mortality and mechanical ventilation utilization amongst COVID-19 hospitalizations-a systematic review and meta-analysis. SN Compr Clin Med. 2020:1–10.
[44] Greenland S, Mansournia MA, Altman DG. Sparse data bias: a problem hiding in plain sight. Bmj. 2016;352:i1981.
[45] Greenland S, Mansournia MA. Penalization, bias reduction, and default priors in logistic and related categorical and survival regressions. Stat Med. 2015;34:3133–43.
[46] Mansournia MA, Geroldinger A, Greenland S, Heinze G. Separation in logistic regression: causes, consequences, and control. Am J Epidemiol. 2018;187:864–70.