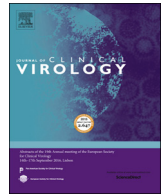




Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Epidemiological characteristics of coronavirus disease 2019 (COVID-19) patients in IRAN: A single center study



Mohamad Nikpouraghdam^a, Alireza Jalali Farahani^b, GholamHossein Alishiri^c, Soleyman Heydari^d, Mehdi Ebrahimnia^e, Hossein Samadinia^f, Mojtaba Sepandi^{g,*}, Nematollah Jonaidi Jafari^g, Morteza Izadi^g, Ali Qazvini^d, Ruhollah Dorostkar^h, Mahdi Tat^h, Alireza Shahriary^c, Gholamreza Farnooshⁱ, Seyed Reza Hosseini Zijoud^b, Maryam Taghdir^g, Yousef Alimohamadi^j, Sepideh Abbaszadeh^g, Hadi Esmaeili Gouvarchin Ghaleh^h, Mahdi Bagheri^{g,k}

^a Nephrology and Urology Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran

^b Atherosclerosis Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran

^c Chemical Injuries Research Center, Systems Biology and Poisonings Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran

^d Trauma Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran

^e Health Management Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran

^f Nanobiotechnology Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran

^g Health Research Center, Life Style Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran

^h Applied Virology Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran

ⁱ Applied Biotechnology Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran

^j Pars Advanced and Minimally Invasive Medical Manners Research Center, Pars Hospital, Iran University of Medical Sciences, Tehran, Iran

^k Student Research Committee, Baqiyatallah University of Medical Sciences, Tehran, Iran

ARTICLE INFO

Keywords:

COVID-19
Epidemiology
Case Fatality Rate
SARS-CoV-2
Comorbidity
IRAN

ABSTRACT

Background: An outbreak of COVID-19 in Iran has spread throughout the country. Identifying the epidemiological characteristics of this disease will help to make appropriate decisions and thus control the epidemic. The aim of this study was characterization of the epidemiological features of COVID-19 in Iran.

Methods: In this retrospective study, data related to the epidemiological characteristics of COVID-19 patients admitted to Baqiyatallah Hospital in Tehran, Iran, from 19 February 2020 to 15 April 2020 have been analyzed and reported. Patient characteristics including age, gender and underlying diseases were investigated. Data were collected through patient records. Sex ratio, Case Fatality Rate (CFR) and daily trend of cases were also determined. A multiple logistic regression analysis was also performed to assess affecting factors on mortality.

Results: From February 19, 2020 to April 15, 2020, 12870 patients referred to the hospital emergency department, of which 2968 were hospitalized with COVID-19 diagnosis. The majority of cases were in the age group of 50 to 60 years of old. The male-to-female ratio was 1.93:1. A total of 239 deaths occurred among all cases for an overall CFR of 1.85% based on the total number of patients (both outpatient and inpatient) and 8.06% among hospitalized patients. Out of all patients 10.89% had comorbidity. Diabetes, chronic respiratory diseases, hypertension, cardiovascular diseases, chronic Kidney diseases and cancer were the most common comorbidities with 3.81, 2.02, 1.99, 1.25, 0.60 and 0.57 %, respectively. Male gender (OR = 1.45, 95% CI: 1.08-1.96), older age (OR = 1.05, 95% CI: 1.04-1.06) and having underlying diseases (OR = 1.53, 95% CI: 1.04-2.24) were significantly associated with mortality.

Conclusions: The results of this study showed that Male gender, older age and having comorbidities were significantly associated with the risk of death among COVID-19 patients. It is important to pay special attention to male elderly patients with underlying diseases.

* Corresponding author.

E-mail address: msepandi@bmsu.ac.ir (M. Sepandi).

<https://doi.org/10.1016/j.jcv.2020.104378>

Received 16 April 2020; Accepted 19 April 2020

1386-6532/ © 2020 Elsevier B.V. All rights reserved.

1. Background

For the first time in late December 2019, cases of pneumonia with an unknown cause were reported in Wuhan, China, and later in January 2020, a new type of coronavirus was identified as the cause of those pneumonia cases [1]. The World Health Organization (WHO) chose the official name of COVID-19 (stand for coronavirus disease 2019), for the disease, as well as the term SARS – COV-2(severe acute respiratory syndrome coronavirus 2) for the virus [2]. A similar to SARS and Middle East Respiratory Syndrome (MERS) coronaviruses trend has been seen in the epidemiology of this emerging disease [3]. In March 11, 2020, the WHO announced COVID-19 as a pandemic [4]. The disease is highly contagious and each infected person could infect at least 3 other people on average [5]. As of, April 15, 2020, 76,389 patients with COVID-19 have been identified in Iran, of which 4777 deaths have been occurred by the virus. According to statistics, Iran ranks sixth after the United States, Italy, Spain, France and the United Kingdom in the number of deaths due to COVID-19 [6]. The first deaths from COVID-19 reported officially on Feb 19, 2020 [7]. Identifying the epidemiological characteristics of this disease will help to make appropriate decisions and thus control the epidemic. Certain epidemiological features of COVID-19 have been previously reported [8–11]. However, these studies were based on relatively small sample sizes, and mostly from China. The aim of this study was characterization of the epidemiological features of COVID-19 in Iran as a country with a population of more than 83 million people [12] in the Middle East and the Persian Gulf region. Here, we report the results of an epidemiological analysis of all cases hospitalized in Baqiyatallah Hospital, affiliated to Baqiyatallah University of Medical Sciences (BMSU), in Tehran, Iran.

2. Method

2.1. Study design and data collection

The present study was a retrospective, epidemiological study that has been performed on hospitalized cases of COVID-19 in Baqiyatallah hospital in Tehran. According to hospital data, patients were admitted from 19 February 2020, to 15 April 2020. All patient information is kept confidential. Patients were confirmed by RT-PCR (Reverse transcription-polymerase chain reaction) using throat and nose swab specimens from the upper respiratory tract or clinically diagnosed based on lung imaging features specially Chest CT(Computed tomography) scan ground glass pathognomonic features consistent with coronavirus pneumonia, depending on the physician's orders. All registered cases at the hospital had a national unique code, so there were no duplicates. The study variables were as follows: gender, age, final outcome (including death or survival), type of comorbidities.

2.2. Statistical analysis

Descriptive analyses of the variables were expressed as mean (\pm Standard Deviation = SD), median (with an interquartile range = IQR = Q_1 - Q_3), or number (%). The analyses were based on non-missing data, and missing data were not imputed. The age and sex distribution were examined and relevant charts were drawn. Sex ratio (male to female) and the case fatality rate (CFR) were calculated. To investigate the effect of age, gender, and comorbidities on mortality, a multiple logistic regression model was used. Adjusted Odds Ratio (OR) with 95 % Confidence Interval (CI) was calculated. The α : 0.05 was considered as a significance level. The data were analyzed using the STATA version 11.0 and Excel version 2010.

3. Results

From February 19, 2020 to April 15, 2020, a total of 12,870 patients referred to the hospital emergency department, of which 2968 were

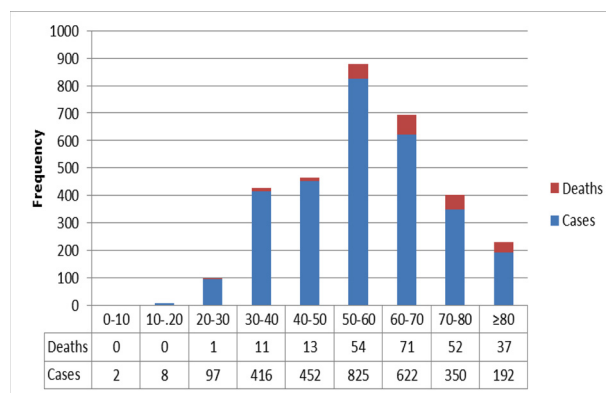


Fig. 1. The distribution of all cases and deaths in each age group (n = 2964).

Table 1 Demographics and characteristics of patients infected with COVID-19.

Variable	Subgroups	All Cases N (%)	Deaths, N	Case Fatality Rate (%)
Overall	–	2964	239	8.06
Age, years	0–10	2(0.07)	0	–
	10–20	8(0.27)	0	–
	20–30	97(3.27)	1	1.03
	30–40	416(14.03)	11	2.64
	40–50	452(15.25)	13	2.87
	50–60	825(27.83)	54	6.54
	60–70	622(20.98)	71	11.41
	70–80	350 (11.80)	52	14.85
	≥80	192(6.50)	37	19.27
Gender	Female	1009(34.00)	72	7.13
	Male	1955(66.00)	167	8.54
Comorbidity	No	2641(89.10)	201	7.61
	Diabetes	113(3.81)	11	9.73
	Chronic respiratory disease	60(2.02)	9	15
	Hypertension	59(1.99)	8	13.55
	Cardiovascular disease	37(1.25)	4	10.81
	Chronic Kidney disease	18(0.60)	3	16.66
	Cancer (any)	17(0.57)	1	5.88
	Other diseases*	19(0.64)	2	10.52
Patient Status†	Recovery	2639(89.03)	–	–
	Hospitalized	86(2.90)	–	–
	Death	239(8.06)	–	–

* Other diseases: Liver disorders, chronic rheumatic diseases, Anemia, Immunodeficiency disorders.

† Recovery refers to patients who have recovered and been discharged. Hospitalized patients are patients who are still hospitalized and under care.

hospitalized with COVID-19 diagnosis. The mean of age was 55.50 ± 15.15 years and the median of age was 56(46–65) years. The majority of cases were in the age group of 50–60 years (Fig. 1). Also, most cases (66 %) were male. The male-to-female ratio was 1.93:1. CFRs are shown in Table 1. Totally 239 deaths occurred during the entire study period, so the overall CFR was calculated to be 1.85 % based on the total number of patients (both outpatient and inpatient) and also CFR was calculated to be 8.06 % among hospitalized patients.

Among the 239 deaths, the mean of age was 65.38 ± 13.67 years and the median of age was 65(57–75) years. A majority (160 = 66.94 %) were ≥ 60 years of age and 38(15.89 %) had comorbidities. Patients over 80 years of age had the highest CFR among the age groups (19.27 %). The CFR was 8.54 % and 7.13 % for men and women, respectively. A total of 323(10.89 %) of patients had chronic underlying diseases. As shown in Fig. 2, Diabetes, chronic respiratory diseases, hypertension, cardiovascular diseases, chronic kidney diseases and cancer were the

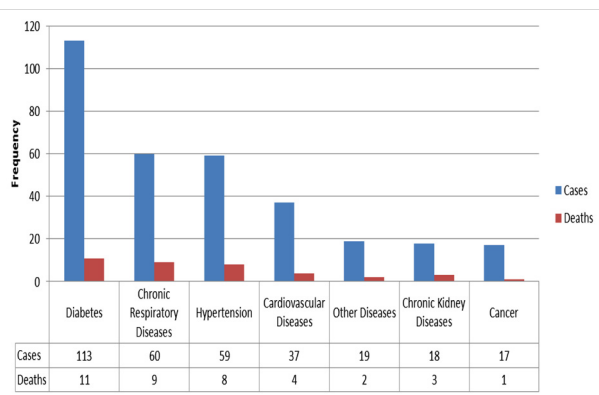


Fig. 2. The distribution of comorbidities among all Covid-19 cases as well as cases that have died.

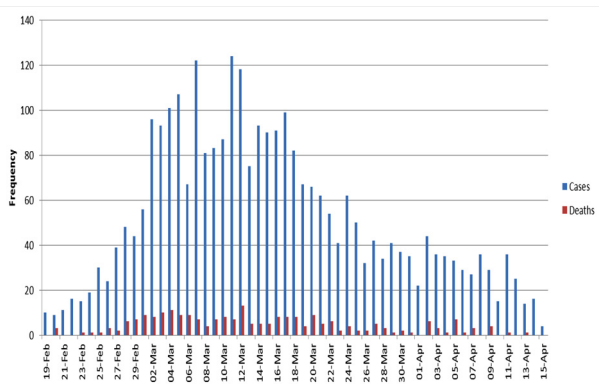


Fig. 3. The distribution of Covid-19 patients according to date of Hospital admission (n = 2964).

Table 2
The effective epidemiological factors on Mortality of Covid-19 Patients.

Variable	Odds Ratio	Standard Error	P-Value	[95 % Confidence Interval]
Comorbidity	1.53	0.19	0.03	1.04 - 2.24
Age	1.05	0.005	< 0.0001	1.04 - 1.06
Male Gender	1.45	0.15	0.01	1.08 - 1.96

most common comorbidities with 3.81, 2.02, 1.99, 1.25, 0.60 and 0.57 %, respectively. While patients who reported no comorbidity had a CFR of 7.61 %, patients with comorbid conditions had higher rates (9.73 % for diabetes, 10.81 % for those with cardiovascular disease, 15 % for those with chronic respiratory disease, and 13.55 % for those with hypertension, 16.66 % for chronic Kidney diseases and 5.88 % for patients with cancer. Fig. 3 indicates the number of cases as well as deaths based on the date of admission from February 19, 2020 to April 15, 2020. The results of logistic regression showed that male gender significantly increased odds of death by 45 % (OR = 1.45, 95 % CI: 1.08–1.96). Also, for a one-year increase in the age, the odds of death increases by 5% (OR = 1.05, 95 % CI: 1.04–1.06). Having underlying disease also increases the odds of mortality by 53 % (OR = 1.53, 95 % CI: 1.04–2.24) this was also statistically significant (Table 2).

4. Discussion

The present epidemiological study on 2964 COVID-19 hospitalized cases between 19 February 2020 to 15 April 2020, provides information about the disease and the outbreak in Iran. As shown in Fig. 1, the increasing trend of hospitalized cases over a short period of time (19

February to March 11) is clear. This finding could confirm the rapid spread of the disease in the population. The peak of hospitalization occurred on March 11, and since March 17, the number of hospitalized cases has decreased slightly. The data appear to indicate a propagated source pattern of spread. Estimates suggest that around 14 % of people infected with COVID-19 have severe disease, and 6% are critically ill [13], hence, about 20 % of all cases of the disease are usually need to be hospitalized. Since Baqiyatallah Hospital is a referral center in Tehran, so, it can be concluded that there is probably a similar trend in the general population. Among the 239 deaths, a majority (160 = 66.94 %) has been ≥ 60 years of age and 38(15.89 %) had comorbidities such as diabetes, hypertension and chronic respiratory diseases and etc. According to the results of our study, overall CFR was calculated to be 1.85 % based on the total number of patients (both outpatient and inpatient). Other studies have been reported CFR ranged from 2.5 % to 3%, [14,15]. CFR was also calculated to be 8.06 % among hospitalized patients, it is not surprising that the CFR among hospitalized patients was high as patients with a better general condition who were not hospitalized and therefore not included in the denominator. A recently published systematic review and meta-analysis reports a CFR of over 13 % in 7 studies describing 632 hospitalized patients [16]. Also, two studies from China, reported a CFR of 15 % [8] and 11 % [9], respectively. Besides, in a study the CFR has been reported to be as high as 49 % among critical hospitalized cases [17]. The results of logistic regression showed the significant effects of age, male gender and underlying diseases on risk of death in patients with COVID-19. In line with other studies [18,19] the regression analysis in our study revealed that older age is associated with higher risk of mortality. Some studies showed that older age is associated with declined immune system ability [20]. Previously, older age has been reported as an associated factor for mortality in SARS [21] and MERS [22]. The present study showed that male gender significantly increases mortality (OR = 1.45, 95 % CI: 1.08–1.96). We also observed a greater number of males than females in the 2964 cases of COVID-19 infection. MERS-CoV and SARS-CoV have also been found to infect more men than women [23,24]. This finding is consistent to other studies [9,25]. The less susceptibility to infection among women could be attributed to the X chromosome and sex hormones, which have been reported to play role in innate and adaptive immunity [26]. Furthermore, according to our results, 10.89 % of patients had chronic underlying diseases, mainly diabetes, chronic respiratory diseases, hypertension and cardiovascular diseases; this is similar to MERS-CoV [24]. In line with other studies [27–29], our result also showed that, having comorbidities had a statistically significant effect on Mortality (OR = 1.53, 95 % CI: 1.04–2.24). A study suggested that compared to patients with no comorbidities, the risk of death in patients with influenza is more than in those who had cardiovascular disease and hypertension [30]. As far as our knowledge shows, the present study is the first descriptive study of the COVID-19 outbreak in Iran, with a large sample size. Although the sample size in the present study is a major advantage, unfortunately, more detailed patient information, particularly regarding clinical outcomes and early symptoms was unavailable at the time of analysis. Importantly, this may limit the conclusions from this data. However, the data in this study permit an early assessment of the epidemiological characteristics of COVID-19 cases in Tehran, Iran. Further studies in outpatient, primary care, or community settings would help to get a full picture of the clinical presentation, natural history, risk factors and the spectrum of clinical severity of the disease. In addition, further efforts should be made to compensate for the above mentioned limitation in future studies. Rapid, reliable and feasible diagnostic tests are important, as well as differential diagnoses based on clinical descriptions by physicians. Careful national surveillance is essential to monitor the disease and its epidemiological characteristics including infectivity, host adaption, viral evolution, transmissibility, and pathogenicity. Efforts and initiatives at the national, regional and global levels need to be made to cut off the disease transmission chain.

5. Conclusion

The results of this study emphasize the significant effect of older age, male gender and underlying diseases on the risk of mortality among COVID-19 patients, which has been mentioned previously in other studies. So it is recommended to take preventative measures more seriously in the elderly patients. Also regarding medical care, it is important to pay special attention to elderly patients who also have underlying diseases. As COVID-19 is considered a global health threat, it still needs to be investigated deeply.

Ethical approval

This study has been approved by the ethics committee of BMSU (Registration code: **IR.BMSU.REC.1399.057**). Data records were anonymous, so informed consent was waived.

Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Funding

No funding was received for this work

CRedit authorship contribution statement

Mohamad Nikpouraghdam: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Writing - original draft, Writing - review & editing. **Alireza Jalali Farahani:** Data curation, Writing - review & editing. **Gholamhossein Alishiri:** Writing - review & editing. **Soleyman Heydari:** Data curation, Writing - review & editing. **Mehdi Ebrahimnia:** Data curation, Validation, Writing - review & editing. **Hossein Samadinia:** Writing - review & editing. **Mojtaba Sepandi:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Software, Supervision, Validation, Visualization, Writing - original draft, Writing - review & editing. **Nematollah Jonaidi Jafari:** Writing - review & editing. **Morteza Izadi:** Writing - review & editing. **Ali Qazvini:** Writing - review & editing. **Ruhollah Dorostkar:** Writing - review & editing. **Mahdi Tat:** Writing - review & editing. **Alireza Shahriary:** Writing - review & editing. **Gholamreza Farnoosh:** Writing - review & editing. **Seyed Reza Hosseini Zijoud:** Writing - review & editing. **Maryam Taghdir:** Data curation, Writing - review & editing. **Yousef Alimohamadi:** Writing - review & editing. **Sepideh Abbaszadeh:** Writing - review & editing. **Hadi Esmaeili Gouvarchin Ghaleh:** Writing - review & editing. **Mahdi Bagheri:** Writing - review & editing.

Declaration of Competing Interest

The authors declare that there are no competing interests.

Acknowledgments

We acknowledge all health-care workers involved in the diagnosis and treatment of patients in Baqiyatallah Hospital affiliated to Baqiyatallah University of Medical Sciences, Tehran, Iran. The authors would like to thank to guidance and advice from the "Clinical Research Development Unit of Baqiyatallah Hospital".

References

- [1] N. Zhu, D. Zhang, W. Wang, X. Li, B. Yang, J. Song, et al., A novel coronavirus from patients with pneumonia in China, 2019, *N. Engl. J. Med.* (2020).
- [2] WHO, Naming the Coronavirus Disease (COVID-19) and the Virus That Causes It, (2020).
- [3] A.R. Fehr, R. Channappanavar, S. Perlman, Middle East respiratory syndrome: emergence of a pathogenic human coronavirus, *Annu. Rev. Med.* 68 (2017) 387–399.
- [4] WHO, novel-coronavirus-2019/events-as-they-happen, (2020).
- [5] Y. Alimohamadi, M. Taghdir, M. Sepandi, The estimate of the basic reproduction number for novel coronavirus disease (COVID-19): a systematic review and meta-analysis, *J. Prev. Med. Public Health* (2020).
- [6] worldometers. 2020.
- [7] A. Takian, A. Raofi, S. Kazempour-Ardebili, COVID-19 battle during the toughest sanctions against Iran, *Lancet* (2020).
- [8] C. Huang, Y. Wang, X. Li, L. Ren, J. Zhao, Y. Hu, et al., Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China, *Lancet* (395) (2020) 497–506.
- [9] N. Chen, M. Zhou, X. Dong, J. Qu, F. Gong, Y. Han, et al., Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study, *Lancet* (395) (2020) 507–513.
- [10] D. Wang, B. Hu, C. Hu, F. Zhu, X. Liu, J. Zhang, et al., Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China, *Jama.* (2020).
- [11] C. Wu, X. Chen, Y. Cai, X. Zhou, S. Xu, H. Huang, et al., Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China, *JAMA Intern. Med.* (2020).
- [12] worldometers, Iran Demographics, (2020).
- [13] R.M. Anderson, H. Heesterbeek, D. Klinkenberg, T.D.J.T.L. Hollingsworth, How will country-based mitigation measures influence the course of the COVID-19 epidemic? *Lancet* 395 (2020) 931–934.
- [14] X. Zhao, B. Zhang, P. Li, C. Ma, J. Gu, P. Hou, et al., Incidence, clinical characteristics and prognostic factor of patients with COVID-19: a systematic review and meta-analysis, *medRxiv.* (2020).
- [15] Z. Wu, J.M. McGoogan, 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).
- [16] A.J. Rodriguez-Morales, J.A. Cardona-Ospina, E. Gutiérrez-Ocampo, R. Villamizar-Peña, Y. Holguin-Rivera, J.P. Escalera-Antezana, et al., Clinical, laboratory and imaging features of COVID-19: a systematic review and meta-analysis, *Travel Med. Infect. Dis.* (2020) 101623.
- [17] 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* (41) (2020) 145.
- [18] S. Zhao, Q. Lin, J. Ran, S.S. Musa, G. Yang, W. Wang, et al., Preliminary estimation of the basic reproduction number of novel coronavirus (2019-nCoV) in China, from 2019 to 2020: A data-driven analysis in the early phase of the outbreak, *Int. J. Infect. Dis.* (2020).
- [19] Z. Cao, Q. Zhang, X. Lu, D. Pfeiffer, Z. Jia, H. Song, et al., Estimating the effective reproduction number of the 2019-nCoV in China, *medRxiv* (2020).
- [20] C. Wu, X. Chen, Y. Cai, X. Zhou, S. Xu, H. Huang, et al., Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China, *JAMA* (2020).
- [21] S.-H. Hong, J.-P. Choi, S.-H. Hong, J. Lee, J.-S. Kwon, S.-M. Kim, et al., Predictors of mortality in Middle East respiratory syndrome (MERS), *Thorax* 73 (2018) 286–289.
- [22] K.W. Choi, T.N. Chau, O. Tsang, E. Tso, M.C. Chiu, W.L. Tong, et al., Outcomes and prognostic factors in 267 patients with severe acute respiratory syndrome in Hong Kong, *Ann. Intern. Med.* 139 (2003) 715–723.
- [23] R. Channappanavar, C. Fett, M. Mack, P.P. Ten Eyck, D.K. Meyerholz, S. Perlman, Sex-based differences in susceptibility to severe acute respiratory syndrome coronavirus infection, *J. Immunol.* 198 (2017) 4046–4053.
- [24] A. Badawi, S.G.J.I. Ryoo, I.D. Jo, Prevalence of comorbidities in the Middle East respiratory syndrome coronavirus (MERS-CoV): a systematic review and meta-analysis, *Int. J. Infect. Dis.* 49 (2016) 129–133.
- [25] W.-j Guan, N.i Z-y, Y. Hu, W.-h Liang, Ou C-q, He J-x, et al., Clinical Characteristics of Coronavirus Disease 2019 in China, (2020).
- [26] S. Jaillon, K. Berthenet, C. Garlanda, Sexual dimorphism in innate immunity, *Clin. Rev. Allergy Immunol.* (2017) 1–14.
- [27] Guan W-j, Liang W-h, Y. Zhao, Liang H-r, Chen Z-s, Li Y-m, et al., Comorbidity and its impact on 1590 patients with Covid-19 in China: a nationwide analysis, *Eur. Respir. J.* (2020).
- [28] B. Li, J. Yang, F. Zhao, L. Zhi, X. Wang, L. Liu, et al., Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China, *Clin. Res. Cardiol.* (2020) 1–8.
- [29] A. Abbatecola, R. Antonelli-Incalzi, COVID-19 spiraling of frailty in older Italian patients, *J. Nutr. Health Aging* (2020) 1.
- [30] D. Mertz, T.H. Kim, J. Johnstone, P.-P. Lam, S.P. Kuster, S.A. Fadel, et al., Populations at risk for severe or complicated influenza illness: systematic review and meta-analysis, *JAMA* 347 (2013) f5061.