Cohort Study

In-hospital mortality in SARS-CoV-2 stratified by sex diffrences: A retrospective cross-sectional cohort study

Mohammed Al-Jarallah [a], Rajesh Rajan [a,*], Raja Dashti [a], Ahmad Al Saber [b], Peter A. Brady [c], Hassan Abdelnaby [d,1], Moudhi Alroomi [e], Wael Aboelhassan [f], Mohammed Abdullah [e], Noor AlNasrallah [g], Bader Al-Bader [h], Haya Malhas [i], Maryam Ramadhan [j], Naser Alotaibi [g], Mohammad Al Saleh [h], Farah Almutairi [h], Kobalava D. Zhanna [k]

[a] Department of Cardiology, Sabah Al Ahmed Cardiac Centre, Al Amiri Hospital, Kuwait City, Kuwait
[b] Department of Mathematics and Statistics, University of Strathclyde, Glasgow, G1 1XH, UK
[c] Department of Cardiology, Illinois Masonic Medical Center, Chicago IL, USA
[d] Department of Endemic and Infectious Diseases, Faculty of Medicine, Suez Canal University, Ismailia, Egypt
[e] Department of Infectious Diseases, Infectious Diseases Hospital, Shuwaikh Medical Area, Kuwait
[f] Department of Medicine, Division of Gastroenterology, Jaber Al Ahmed Hospital, South Surra, Kuwait
[g] Department of Medicine, Al Adan Hospital, Hadiya, Kuwait
[h] Department of Medicine, Farwaniya Hospital, Farwaniya, Kuwait
[i] Department of Emergency Medicine, Mubarak Al-Kabeer Hospital, Jabriya, Kuwait
[j] Department of Obstetrics and Gynaecology, Maternity Hospital, Shuwaikh Medical Area, Kuwait
[k] Department of Internal Medicine with the Subspecialty of Cardiology and Functional Diagnostics Named After V.S. Moiseev, Institute of Medicine, Peoples' Friendship University of Russia (RUDN University), Moscow, Russian Federation
[l] Department of Medicine, Division of Gastroenterology, Al Sabah Hospital, Shuwaikh Medical Area, Kuwait

ABSTRACT

Background: The aim of this study was to determine in-hospital mortality in patients presenting with severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) and to evaluate for any differences in outcome according to sex differences.

Methods: Patients with SRS-CoV-2 infection were recruited into this retrospective cohort study between February 26 and September 8, 2020 and stratified according to the sex differences.

Results: In total of 3360 patients (mean age 44 ± 17 years) were included, of whom 2221 (66%) were male. The average length of hospitalization was 13 days (range: 2–31 days). During hospitalization and follow-up 176 patients (5.24%) died. In-hospital mortality rates were significantly different according to gender (p=<0.001). Specifically, male gender was associated with significantly greater mortality when compared to female gender with results significant at an alpha of 0.05, LL = 28.67, df = 1, p = 0.001, suggesting that gender could reliably determine mortality rates. The coefficient for the males was significant, $B = 1.02$, $SE = 0.21$, $HR = 2.78$, $p < 0.001$, indicating that an observation in the male category will have a hazard 2.78 times greater than that in the female category. Multivariate logistic regression confirmed male patients admitted with SARS-CoV-2 had higher cumulative all-cause in-hospital mortality (6.8% vs. 2.3%; adjusted odds ratio (aOR), 2.80; 95% (CI): [1.61–5.03]; p < 0.001).

Conclusions: Male gender was an independent predictor of in-hospital mortality in this study. The mortality rate among male SARS-CoV-2 patients was 2.8 times higher when compared with females.

1. Background

In-hospital mortality in patients affected with SARS-CoV-2

reportedly ranges from 17% to 77% [1–3]. Recent data from 38 countries suggests that mortality may be up to 1.7 times higher males than in females [4]. The prevalence of SARS-CoV-2 infection was also

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reportedly higher in males compared with females [5,6]. Previous studies in patients admitted with MERS and SARS-CoV have also reported a higher mortality amongst males [7,8], who appear to be more susceptible to infection than females [9]. One contributory factor may be smoking history which is more prevalent amongst males [10]. The lower incidence of SARS-CoV-2 in females may also be related to oestrogen-related protection and X-linked gene-related immune responses [11,12]. The aim of this study was to determine in-hospital mortality in patients presenting with acute respiratory syndrome corona virus 2 (SARS-CoV-2) and to evaluate for any differences in outcome according to sex differences.

2. Methods

All patients aged 18 and older diagnosed with SRS-CoV- between February 26 and September 8, 2020 were included both Kuwaitis and non-Kuwaitis into this retrospective cross-sectional cohort study. All data were abstracted from electronic medical records of two tertiary care hospitals in Kuwait: Jaber Al-Ahmed Hospital and Al-Adan General Hospital [13,14]. A positive RT-R swab from the nasopharynx confirmed SRS-oV-2 infection. All patients were treated with a standard universal protocol according to The Ministry of Health, Kuwait. The research was retrospectively registered, the standing committee for health coordination and medical research at the Ministry of Health in Kuwait approved the study protocol and accepted the request for waiver of the consent (Registered as **MOH/108-1422**). This study is registered with Research Registry UIN: researchregistry8002 (https://www.researchregistry.com/register-now#home/registrationdetails/62a6e4071a43e3001eceeeef/).

The primary endpoint was in-hospital mortality due to COVID-19, as specified by ID 10 code U07.1. The collected data comprised socioeconomic factors, co-morbidities, clinical presentation, on admission test results, and ICU and hospital admission duration. For data entry, an electronic case-record form (CRF) was employed. This work has been reported in line with the STROCSS criteria [15].

3. Statistical analysis

Descriptive statistics were used to summarise clinical data. Categorical variables were presented as frequencies and percentages, and the Pearson's $\times 2$ test used to analyse them. Continuous variables were summarized as mean and standard deviation. Multivariate logistic regression was performed to identify the impact of gender on all-cause mortality. Input vairables included gender, age, neutrophils, platelet count, and hemoglobin were used to adjust the odds ratios (oRs) for in-hospital all-cause mortality outcome. A Cox proportional hazards model was utilised to see if gender had a major impact on the risk of mortality. The significance threshold was set at $p < 0.05$. R statistical packages [16] and SPSS version 27 (SPSS, Chicago, IL, US) were used to perform statistical analyses.

4. Results

A total of 3360 study participants were included. The mean age was 44 ± 17 years, and 2221 (66%) of the patients were males. The median length of hospital stay was 13 (range 2–31) days. In this cohort 176 patients (5.24%) died with significantly higher mortality in males (p=<0.001) (Table 1).

When compared to females, males had significantly higher hemoglobin (132 *vs* 177 g/L; $p < 0.001$), white blood cell (8.1 *vs* 7.3 10^9/L; $p < 0.001$) and neutrophil (57 *vs* 54/mcL; $p < 0.001$) counts, prothrombin (15.6 *vs* 14.6 s; $p = 0.016$) and activated partial thromboplastin (37.8 *vs* 35.4 s; $p = 0.047$) times, as well as international normalized ratio(1.2 *vs* 1.1 10^9/L; $p = 0.016$) (Table 2).

Mortality was higher in individuals with lower hemoglobin (124, 22.4%) when compared to individuals with higher hemoglobin (52,

Table 1
Demographics and clinical characteristics of the cohort stratified by gender among patients admitted with SARS-CoV 2.

Characteristic	All	Female	Male	p-value	N
	N = 3360	n = 1139	n = 2221		
Age, Mean ± SD, years	44 ± 17	43 ± 19	44 ± 16	0.093	3360
ICU admission, median (IQR), days	0 (0–4)	0(0–2)	0(0–4)	<0.001	3360
Length of hospital stay, median (IQR), days	13 (2–31)	14 (2–29)	13 (2–32)	0.002	2900
ICU to discharge, median (IQR), days	9 (0–39)	6(0–23)	10 (0–39)	0.008	416
Admission to ICU, median (IQR), days	1.5 ± 2.9	1.4 ± 2.1	1.5 ± 3.0	0.684	257
Mortality, n (%)	176 (5.2%)	26 (2.3%)	150 (6.8%)	<0.001	3360

SD, standard deviation; ICU, intensive care unit; IQR, interquartile range. Percentages might not add up to 100% due to rounding off.

Table 2
Laboratory investigations stratified by gender.

Characteristic, mean ± SD	All N = 3360	Female n = 1139	Male n = 2221	p-value	N
Hemoglobin, g/L	127 (21.7)	117(15.1)	132(22.8)	<0.001	3360
WBC count, 10^9/L	7.85 (4.74)	7.34(3.76)	8.12 (5.15)	<0.001	3345
Neutrophils,/mcL	56.0 (15.1)	54.2(14.4)	56.9 (15.4)	<0.001	3344
Platelets, 10^9/L	305(120)	306(110)	304(125)	0.69	3345
Prothrombin time, sec	15.3 (5.98)	14.6(4.56)	15.6 (6.49)	0.016	851
INR	1.14 (0.49)	1.09(0.37)	1.17 (0.54)	0.016	851
aPTT, sec	37.1 (16.6)	35.4(14.0)	37.8 (17.6)	0.047	799

SD, standard deviation; WBC, white blood cell count; INR, international normalized ratio; APTT, activated partial thromboplastin time.

0.82%; p 0.001). Individuals with a hemoglobin level less than 100 g/L had a greater cumulative all-cause in-hospital mortality than those with hemoglobin levels higher than 100 g/L (22.4% vs. 0.8%; R, 0.29; 95% CI: [0.18–0.46]; p 0.001). In-hospital mortality was associated with a higher neutrophil count [aOR, 1.17; 95% CI:(1.14–1.20, p0.001) and a lower platelet count [aOR, 1.00; 95% I:(1.00–1.00, p = 0.005). With respect to all-cause cumulative in-hospital mortality, age had no significant impact among the groups (aOR, 1.00; 95% CI [0.98–1.02]; p 0.960) (Table 3). Male gender had a large impact on cumulative all-cause in-hospital mortality (6.8% vs. 2.3%) [R, 2.80; 95% CI: [1.61, 5.03]; p 0.001) (Table 3).

Kaplan-Meier survival probability plots were used for the analysis based on gender. Each plot depicts the survival probabilities of various groups over time. Male sex was related to increased mortality (Kaplan-Meier survival probability plot). The model's results were significant and could not be explained by an alpha of 0.05, LL = 28.67, df = 1, p = 0.001, showing that gender could appropriately estimate the risk of mortality. The coefficient for male gender was significant, B = 1.02, SE = 0.21, HR = 2.78, p.001p < 0.001, indicating that male gender was associated with risk of mortality 2.78 times greater than female gender at any given point in time. Gender was observed to be important in predicting in-hospital mortality among SRS-oV-2 patients in this study [Fig. 1].

5. Discussion

The main finding of our study is that male gender is an independent

Table 3
Predictors of in-hospital mortality by univariate and multivariate logistic regression.

In-hospital mortality		Alive	Dead	Univariate OR (95% CI, p-value)	Multivariate logistic regression aOR (95% CI, p-value)
Gender, n (%)					
	Female	1113 (97.7)	26 (2.3)	–	–
	Male	2071 (93.2)	150 (6.8)	3.10 (2.07–4.83, p < 0.001)	2.80(1.61–5.03, p < 0.001)
Age, years	Mean ± SD	43 ± 17	57 ± 12	1.05 (1.04–1.06, p < 0.001)	1.00(0.98–1.02, p = 0.960)
Netrophils, %	Mean ± SD	55 ± 13.6	87 ± 8	1.23 (1.20–1.26, p < 0.001)	1.17(1.14–1.20, p < 0.001)
Platelets, 10^9/L	Mean ± SD	288 ± 103	217 ± 151	0.99 (0.99–0.99, p < 0.001)	1.00(1.00–1.00, p = 0.005)
Hemoglobin, g/L					
	HB ≤ 100	430 (77.6)	124 (22.4)	–	–
	HB > 100	6325 (99.2)	52 (0.8)	0.03 (0.02–0.04, p < 0.001)	0.29(0.18–0.46, p < 0.001)

Number in data frame = 6931, Number in model = 3344, Missing = 3587, AIC = 554.1, *C*-statistic = 0.976, H&L = Chi-sq(8) 2.97 (*p* = 0.936).
OR, odds ratio; aOR, adjusted odds ratio; CI, confidence interval;.
Multivariable analyses were conducted using logistic regression models utilizing the simultaneous method. The models were adjusted for gender, age, neutrophils, hemoglobin, and platelet.
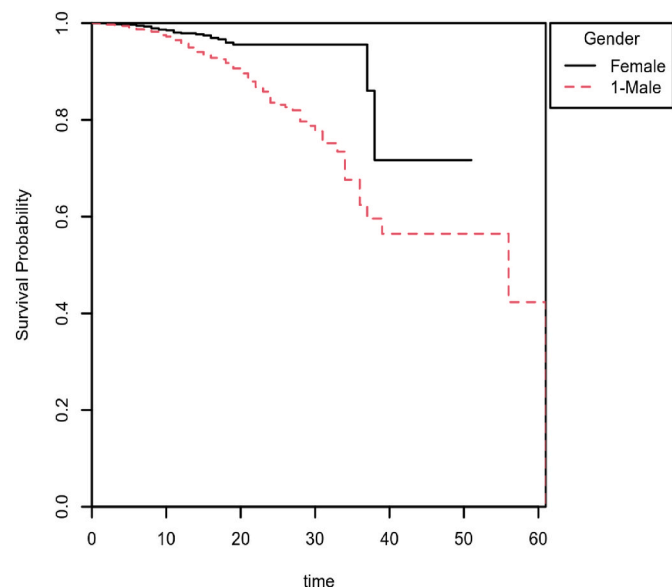
Fig. 1. Kaplan-Meier survival plot of Mortality grouped by Gender Cox Proportional Hazards Regression Coefficients for Gender.

predictor of in-hospital mortality in patients diagnosed with SARS-CoV-2. Specifically, mortality in males with SARS-CoV-2 was 2.8 times higher than in females. Moreover, average length of ICU stay was longer in males. Although older in age, especially middle age and above, had higher mortality, this did not reach statistical significance. A higher neutrophil count and a lower platelet count had a significant impact on in-hospital mortality. The mortality rate was also seen higher in those with lower hemoglobin levels, which has been reported previously [17].

Reasons for these findings most probably relate to severity of infection and the extent of immune response that could be associated with increase in mortality.

One reason for higher mortality observed in males could be the higher prevalence of ACE-2 in the lungs [18]. Oestrogen-related protection in females may suppress SARS-CoV-2, thereby leading to lower mortality [19,20]. The male to female ratio observed in our study was higher than that in prior studies (1.5:1) [21,22]. The significance of gender is equally important as other risk factors in SARS-CoV-2 infection [23]. Several studies have reported higher mortality from SARS-CoV-2 in males. For example, in 144,279 patients in England and Wales significantly higher mortality was observed in males [24]. Similar findings were reported in Europe and Wuhan [25,26]. In addition, a study from Italy reported lower mortality in hospitalized females, but similar mortality among males and females in critically ill SARS-CoV-2 patients [27]. while more critically ill male patients were seen in a study conducted in Europe [28].

Delays in admission have also contributed to an increased rate of mortality in male patients in the setting of SARS-CoV-2 [29]. Younger males and elderly females were the most vulnerable in terms of mortality [30]. In a systematic review and meta-analysis, it was evident that both alcohol consumption and smoking increase mortality in males and females [31].

Our study does have some limitations. First, the study is retrospective limiting causal inference while unmeasured confounding factors, such as clinical co-morbidities and medications, could have affected the outcomes. As this study mainly focused on the sex differences and related in-hospital mortality, we did'nt do any adjustment for comorbidities. Our study was focused towards only in-hospital mortality and hence the available clinical variables were limited.

6. Conclusions

This study demonstrated that gender is an independent predictor of in-hospital mortality in SARS-CoV-2 patients with males 2.8 times more likely to die than females. Despite males having a shorter overall hospitalization than females, males spent a greater proportion of time in intensive care unit. More prospective studies are required to better understand sex-related morbidity and mortality.

Provenance and peer review

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Conflict of interest disclosure

No conflict of interest exists for any author on this manuscript.

Ethics approval statement

This study was approved by the ethics committee and Ministry of Health Kuwait.

Patient consent statement

Patient consented was not mandated for this retrospective observational study. Permission to reproduce material from other sources: No material from other sources is included in this study.

Clinical trial registration

This study was not a clinical trial.

Ethical Approval

Ethics Committee Approval 1081422

Consent

The standing committee for health coordination and medical research at the Ministry of Health in Kuwait approved the study protocol and accepted the request for waiver of the consent (Institutional the requirement of informed \1081422).

Author contribution

MAJ participated in analysis and manuscript preparation. RR participated in data analysis and manuscript preparation. AAS and JP did the statistical analysis as well as manuscript review. All authors had access to data and take responsibility for the integrity of data and the accuracy of data analysis. All authors have read and approved the manuscript.

Registration of Research Studies

1. Name of the registry: Not a registry
2. Unique Identifying number or registration ID: Not applicable
3. Hyperlink to your specific registration (must be publicly accessible and will
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Guarantor

Dr. Rajesh Rajan MD, Ph.D, FRCP(Lon), FRCP(Edin), FRCP (Glasg), FRCP (Ire), FACC, FESC,
FAHA
Department of Cardiology,
Sabah Al Ahmed Cardiac Centre, Al Amiri Hospital
Kuwait City, Kuwait, 15003
Email: cardiology08@gmail.com
Tel: +965-65873326

Data availability

The data are not publicly available due to privacy or ethical restrictions.

Abbrevations

SARS-CoV-2 Severe acute respiratory syndrome coronavirus 2
ICU   Intensive Care Unit
RT-PCR   Reverse Transcription Polymerase Chain Reaction
CI   Confidence Interval
aOR   Adjusted Odds Ratio
CRF   Case Record Form

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.104026.

References

[1] C. Karagiannidis, C. Mostert, C. Hentschker, T. Voshaar, J. Malzahn, G. Schillinger, et al., Case characteristics, resource use, and outcomes of 10 021 patients with COVID-19 admitted to 920 German hospitals: an observational study, Lancet Respir. Med. 8 (2020) 853–862.

[2] S.A. Namendys-Silva, A. Gutiérrez-Villaseñor, J.P. Romero-González, Hospital mortality in mechanically ventilated COVID-19 patients in Mexico, Intensive Care Med. 46 (2020) 2086–2088.

[3] P.C. Hallal, F.P. Hartwig, B.L. Horta, M.F. Silveira, C.J. Struchiner, L.P. Vidaletti, et al., SARS-CoV-2 antibody prevalence in Brazil: results from two successive nationwide serological household surveys, Lancet Global Health 8 (2020) e1390–e1398.

[4] E.P. Scully, J. Haverfield, R.L. Ursin, C. Tannenbaum, S.L. Klein, Considering how biological sex impacts immune responses and COVID-19 outcomes, Nat. Rev. Immunol. 20 (2020) 442–447.

[5] J. Sha, G. Qie, Q. Yao, W. Sun, C. Wang, Z. Zhang, et al., Sex differences on clinical characteristics, severity, and mortality in adult patients with COVID-19: a multicentre retrospective study, Front. Med. 8 (2021), 607059.

[6] T. Haitao, J.V. Vermunt, J. Abeykoon, R. Ghamrawi, M. Gunaratne, M. Jayachandran, et al., COVID-19 and sex differences: mechanisms and biomarkers, Mayo Clin. Proc. 95 (2020) 2189–2203.

[7] I. Alghamdi, I. Hussain, M. Alghamdi, S. Almalki, M. Alghamdi, M. Elsheemy, The pattern of Middle East respiratory syndrome coronavirus in Saudi Arabia: a descriptive epidemiological analysis of data from the Saudi Ministry of Health, Int. J. Gen. Med. 7 (2014) 417–423.

[8] J. Karlberg, D.S. Chong, W.Y. Lai, Do men have a higher case fatality rate of severe acute respiratory syndrome than women do? Am. J. Epidemiol. 159 (2004) 229–231.

[9] S.L. Klein, K.L. Flanagan, Sex differences in immune responses, Nat. Rev. Immunol. 16 (2016) 626–638.

[10] H. Cai, Sex difference and smoking predisposition in patients with COVID-19, Lancet Respir. Med. 8 (2020), e20.

[11] 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.

[12] D.P. Robinson, S.A. Huber, M. Moussawi, B. Roberts, C. Teuscher, R. Watkins, et al., Sex chromosome complement contributes to sex differences in coxsackievirus B3 but not influenza A virus pathogenesis, Biol. Sex Differ. 2 (2011) 8.

[13] M. Al-Jarallah, R. Rajan, R. Dashti, A. Al Saber, J. Pan, K.D. Zhanna, H. Abdelnaby, W. Aboelhassan, F. Almutairi, M. Abdullah, N. Alotaibi, M. Al Saleh, N. Al Nasrallah, B. Al-Bader, H. Malhas, M. Ramadhan, P.A. Brady, I. Al-Zakwani, M. Alroomi, In-hospital mortality in SARS-CoV-2 stratified by serum 25-hydroxy-vitamin D levels: a retrospective study, J. Med. Virol. 7 (2021 Jun), https://doi.org/10.1002/jmv.27133. Epub ahead of print, 34101207.

[14] M. Al-Jarallah, R. Rajan, R. Dashti, A. Al Saber, J. Pan, K.D. Zhanna, H. Abdelnaby, W. Aboelhassan, F. Almutairi, M. Abdullah, N. Alotaibi, M. Al Saleh, N. Al Nasrallah, B. Al-Bader, H. Malhas, M. Ramadhan, M. Hamza, P.A. Brady, I. Al-Zakwani, M. Alroomi, In-hospital mortality in SARS-CoV-2 stratified by serum 25-hydroxy-vitamin D levels: a retrospective study, J. Med. Virol. 93 (10) (2021) 5880–5885, https://doi.org/10.1002/jmv.27133.

[15] G. Mathew, R. Agha, for the STROCSS Group, Strocss 2021: strengthening the Reporting of cohort, cross-sectional and case-control studies in Surgery, Int. J. Surg. 96 (2021), 106165.

[16] T. Laine, E.M. Reyes, Tutorial: survival estimation for Cox regression models with time-varying coefficients using SAS and R, J. Stat. Software 61 (2014) 1–23.

[17] M. Al-Jarallah, R. Rajan, AAl Saber, J. Pan, A.T. Al-Sultan, H. Abdelnaby, et al., In-hospital mortality in SARS-CoV-2 stratified by hemoglobin levels: a retrospective study, eJHaem (2021) 1–5.

[18] Y. Zhao, Z. Zhao, Y. Wang, Y. Zhou, Y. Ma, W. Zuo, Single-cell RNA expression profiling of ACE2, the putative receptor of Wuhan 2019-nCov, bioRxiv (2020), https://doi.org/10.1101/2020.01.26.919985.

[19] J. Jin, P. Bai, W. He, F. Wu, X. Liu, D. Han, et al., Gender differences in patients with COVID-19: focus on severity and mortality, Front. Public Health 8 (2020) 152.

[20] 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.

[21] S. Richardson, J.S. Hirsch, M. Narasimhan, J.M. Crawford, T. McGinn, K.W. Davidson, et al., Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area, JAMA 323 (2020) 2052–2059.

[22] M.R. Mehra, S.S. Desai, S. Kuy, T.D. Henry, A.N. Patel, Cardiovascular disease, drug therapy, and mortality in Covid-19, N. Engl. J. Med. 382 (2020) 2582.

[23] P.A. Spagnolo, J.E. Manson, H. Joffe, Sex and gender differences in health: what the COVID-19 pandemic can teach us, Ann. Intern. Med. 173 (2020) 385–386.

[24] M.O. Mohamed, C.P. Gale, E. Kontopantelis, T. Doran, M. de Belder, M. Asaria, et al., Sex differences in mortality rates and underlying conditions for COVID-19 deaths in England and Wales, Mayo Clin. Proc. 95 (2020) 2110–2124.

[25] L.J. Ahrenfeldt, M. Otavova, K. Christensen, R. Lindahl-Jacobsen, Sex and age differences in COVID-19 mortality in Europe, Wien Klin. Wochenschr. 133 (2021) 393–398.

[26] J. Chen, H. Bai, J. Liu, G. Chen, Q. Liao, J. Yang, et al., Distinct clinical characteristics and risk factors for mortality in female inpatients with coronavirus disease 2019 (COVID-19): a sex-stratified, large-scale cohort study in wuhan, China, Clin. Infect. Dis. 71 (2020) 3188–3195.

[27] F. Raimondi, L. Novelli, A. Ghirardi, et al., Covid-19 and gender: lower rate but same mortality of severe disease in women—an observational study, BMC Pulm. Med. 21 (2021) 96.

[28] C. Gebhard, V. Regitz-Zagrosek, H.K. Neuhauser, R. Morgan, S.L. Klein, Impact of sex and gender on COVID-19 outcomes in Europe, Biol. Sex Differ. 11 (2020) 29.

[29] C. Ma, J. Gu, P. Hou, L. Zhang, Y. Bai, Z. Guo, et al., Incidence, clinical characteristics and prognostic factor of patients with COVID-19: a systematic

review and meta-analysis, MedRxiv (2020), https://doi.org/10.1101/2020.03.17.20037572.

[30] National Center for Health Statistics. Centers for Disease Control and Prevention, M.D. Bethesda, Provisional COVID-19 Death Counts by Sex, Age, and State 2020, 2020. https://data.cdc.gov/NCHS/Provisional-COVID-19-Deaths-by-Sex-and-Age/9bhg-hcku.

[31] B.B. Abate, A.M. Kassie, M.W. Kassaw, T.G. Aragie, S.A. Masresha, Sex difference in coronavirus disease (COVID-19): a systematic review and meta-analysis, BMJ Open 10 (2020), e040129.