



Original Article:



Sex and age Differences in Hospitalization and Mortality Rates Due to COVID-19 from 20 March 2020 until 20 March 2022 in Iran: A Population-based Study

Salman Daneshi^{1,2} , Saied Bokaie^{3*} , Alireza Bahonar³, Ali Akbar Haghdoost⁴, Eshagh Barfar⁵, Cain C. T. Clark⁶

1. Ph.D. Student of Epidemiology, Department of Food Hygiene and Quality Control, Division of Epidemiology & Zoonoses, Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran.
2. Department of Public Health, School of Health, Jiroft University of Medical Sciences, Jiroft, Iran.
3. Department of Food Hygiene and Quality Control, Division of Epidemiology & Zoonoses, Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran.
4. Research Center for Modeling in Health, Institute for Future Studies in Health, Kerman University of Medical Sciences, Kerman, Iran.
5. Health Promotion Research Center, Zahedan University of Medical Sciences, Zahedan, Iran.
6. Institute for Health and Wellbeing, Coventry University, Coventry, UK.



Cite this article as: Daneshi S, Bokaie S, Bahonar A, Haghdoost AA, Barfar E, C. T. Clark C. Sex and age Differences in Hospitalization and Mortality Rates Due to COVID-19 from 20 March 2020 until 20 March 2022 in Iran: A Population-based Study. Archives of Advances in Biosciences. 2023; 14:E40101. <https://doi.org/10.22037/aab.v14i.40101>

 <https://journals.sbmu.ac.ir/aab/article/view/40101>



Article info:

Received: 21 Dec 2022

Accepted: 03 Jan 2023

Published: 08 Sep 2023

*** Corresponding author:**

Saied Bokaie, PhD.

Address: Department of Food Hygiene and Quality Control, Division of Epidemiology & Zoonoses, Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran.

E-mail: sdbokaie@gmail.com

Abstract

Introduction: This study aimed to identify the effect of differences in age-sex structure in COVID-19 hospitalizations and death rates among men and women in Iran. Accordingly, we calculated the SARS-CoV-2 hospitalized patients and mortality rates, stratified by sex, age, and demographic distribution.

Materials and Methods: This was a cross-sectional study, where the target population was the total population from 20 March 2020 until 20 March 2022 in Iran, over the two-time periods, 20 March 2020 until 20 March 2021 [first year], and 20 March 2021 until 20 March 2022 [second year]. The chi-squared test was used for analysis.

Results: During the first year, 493220 cases were hospitalized with 258209 (52%) men, in addition 61,586 deaths occurred, where 34,849 [57%] were men. The overall hospitalization rate per 100,000 population in men and women was 607.77 and 565.57, respectively, and the mortality rate per 100,000 population in men and women was 82.03 and 64.34, respectively. During the second year, 652893 cases were hospitalized, where 340344 (52%) were women. The overall hospitalization rate per 100,000 population in men and women was 727.98 and 809.67, respectively, in addition to 54,740 deaths, where 29,172 [53%] were men. The overall mortality rate per 100,000 population in men and women was 67.95 and 60.83, respectively.

Conclusion: The findings showed a higher hospitalization in the first year in men, whilst the opposite was evident in the second year. The mortality rate increased with age and was most predominant in men, 50 years of age or older. Therefore, there is a need for policy makers to be acutely aware of the discrepancies in mortality according to age and sex groups, and have different, and complementary, strategies for controlling the pandemic by age and sex groups.

Keywords: COVID-19, Hospitalization rate, Iran Mortality, Rate

1. Introduction

A novel Coronavirus subtype emerged in Wuhan [Hubei, China], in December 2019, with infection outbreaks across China and around the world. By the beginning of March 2020, cases of COVID-19 had been confirmed in most regions throughout the world [1], with a variety of clinical signs and different outcomes [2, 3]. Data from early reported cases in China suggested that the mortality rate from COVID-19 was higher for infected men than for infected women [4, 5]. Moreover, studies in China, South Korea, the United States, and Italy have reported that case fatality rates of COVID-19 patients are higher in male patients than in female patients [5-7]. Indeed, several countries with available data have shown higher infection, mortality, and fatality rates in males than in females, and these rates varied from country to country and between regions [8-10]. The previous outbreaks of coronaviruses, Severe Acute Respiratory Syndrome [SARS], and Middle East Respiratory Syndrome [MERS], yielded Comparable findings of differences in mortality between age and sex [5]. A study showed fatality rates of 2.8% in men versus 1.7% in women [5]. However, sex differences varied between regions and were age-dependent with significant differences among patients aged 30 years and above. A review of epidemiological data on confirmed COVID-19 cases in Europe and China until 1 April 2020 found that the male-to-female COVID-19 case fatality rates (CFRs) reported from France, Italy, Spain, Germany, Switzerland, and China were relatively homogeneous and ranged between 1.7 and 1.8 [11]. In addition, pooled data from Italy, Spain, Germany, and Switzerland, comprising 227,219 confirmed cases and 14,364 deaths, suggested that although male-to-female CFR was consistently elevated through all age groups, the sex difference was most pronounced at middle age, particularly at ages 50-59 years [11]. Correspondingly, data on COVID-19 cases and deaths obtained from outbreaks in China, Italy, and New York City demonstrated higher mortality for men than for women all ages [12]. In the present study, we examine the magnitude of sex differences in survival from COVID-19 across age groups and regions in Iran. This will enable us to investigate the consistency of sex differences across regions and thus map the epidemiology of the disease; however, due to the highly variable rate of COVID-19 by age, the age-specific mortality from COVID-19 is considered. We hypothesized that men would have higher mortality than women at any given age, but that sex differences in mortality from COVID-19 would decrease with age [13]. The purpose of this study was to identify the differences in age-sex structure and demographic

distribution in hospitalization and mortality rates due to COVID-19 in Iran.

2. Materials and Methods

Study protocol

This study was conducted using a cross-sectional design. The target population of this study was the total population from 20 March 2020 until 20 March 2022 in Iran, over the two time periods: 20 March 2020 until 20 March 2021 [first year], and 20 March 2021 until 20 March 2022 [second year]. Data in this study includes the routine surveillance of deaths and inclusion criteria in this study were COVID-19 cases which were confirmed through RT-PCR tests and there were no exclusion criteria. Data were received from the Disease Management Center of the Ministry of Health of Iran after obtaining ethics approval.

Data analysis

In this study, age-specific mortality rates were calculated by dividing deaths attributed to COVID-19 in the underlying population count, according to age and sex per 100,000 population. We calculated indexes in this study using Microsoft Excel 2020 considering the following formulas (1,2,3,4) [14] in age and sex groups:

$$\text{formula 1: hospitalized Rate in Age Group} = \frac{\text{Number of hospitalized reported}}{\text{Total population in age Groups}} \times 100000$$

$$\text{formula 2: hospitalized Rate in sex Group} = \frac{\text{Number of hospitalized reported}}{\text{Total population in sex Groups}} \times 100000$$

$$\text{formula 3: Mortality Rate in Age Group} = \frac{\text{Number of death reported}}{\text{Total population in age Groups}} \times 100000$$

$$\text{formula 4: Mortality Rate in sex Group} = \frac{\text{Number of death reported}}{\text{Total population in sex Groups}} \times 100000$$

For comparison of hospitalization and death rates between males and females, and between two years of study, using a chi-squared test. Data were analyzed using SPSS version 20, with an a prior alpha level of 0.05s. This study was approved by the committee of ethics of Jiroft University of Medical Sciences with the ethic code: IR.JMU.REC.1400.036.

3. Results

General findings of the study Findings related to hospitalization

The total number of deaths during the study period

was 1146113, 575355 [50.20%] cases were women, and 493220 [43%] occurred during the first year of the study and the rest during the second year.

Findings related to death

The total number of deaths during the study period was 116,326, of which 64,021 [55%] cases were men, and the rest were women; 61,586 [53%] occurred during the first year of the study and the rest during the second year.

Findings of the first year of study [20 March 2020 until 20 March 2021]

Findings related to hospitalization

During the first year of the study, 493220 cases were hospitalized, and 258209 (52%) were men. The overall hospitalization rate per 100,000 population in men and women was 607.77 and 565.57, respectively. The highest hospitalization rate in men per 100,000 population is in the age groups 79 -75 (3544.98), 70-74 (2772.74), above 80 (2708.30), and 65-69 (2112.79) years, respectively, and the lowest in the age groups 5-9 (35.74), 10-14 (40.94), 15-19 (79.41) and then 4-0 (58.58), respectively. The highest hospitalization rate in women per 100,000 population was in the age groups 75-79 (3151.79), 74-70 (2606.01), over 80 (2102.30), and 65-69 (1982.37) years, respectively, and the lowest was in the age groups 5-9 (30.49), 10-14 [34.89], 20-24 (46.84), and 0-4 (46.84), respectively. The differences between age groups were significant according to chi-square analysis ($P < 0.05$), however, there was no significant differences between men and women.

Findings related to death

During the first year of the study, there were 61,586 deaths, where 34,849 (57%) were men and the rest were women. The overall mortality rate per 100,000 population in men and women was 82.03 and 64.34, respectively. The highest mortality rate in men per 100,000 population was in the age groups above 80 (1898.11), followed by 79 -75 (987.08), 70-74 (663.71), and 65-69 (134.38) years, respectively, and the lowest in the age groups 5-9 (1.33), 10-14 (1.43), 15-19 (3.28), and 4-0 (4.21), respectively. The highest death rate in women per 100,000 population was in age groups over 80 (1309.96), followed by 75-79 (781.92), 74-70 (524.30), and 65-69 (318.46) years, respectively, and the lowest was in the age groups 5-9 (0.96), 10-14 [1.26], 15-19 (2.80) and then 20-24 (3.65), respectively. The differences between age and sex groups were significant according to chi-square

analysis ($P < 0.05$).

Table 1 shows hospitalized and mortality rates per 100,000 population by age and sex in the first year of the study.

Findings of the second year of study [20 March 2021 until 20 March 2022]

Findings related to hospitalization

During the first year of the study, 652893 cases were hospitalized, and 340344 (52%) were women. The overall hospitalized rate per 100,000 population in men and women was 727.98 and 809.67, respectively. The highest hospitalization rate in men per 100,000 population is in the age groups 79 -75 (3777.96), 70-74 (2904.15), above 80 (2628.41), and 65-69 (2459.78) years respectively, and the lowest in the age groups 10-14 (75.79), 5-9 (86.03), 15-19 (120.16) and then 4-0 (239.14) respectively. The highest hospitalization rate in women per 100,000 population was in age groups 75-79 (3663.88), 74-70 (2976.38), 65-69 (2544.92) years, over 80 (2309.28), respectively, and the lowest was in the age groups 10-14 [65.81], 5-9 (68.02), and then 0-4 (119.36), respectively.

The differences between age groups were significant according to chi-square analysis ($P < 0.05$), but there was no significant differences between men and women.

Findings related to death

During the second year of the study, there were 54,740 deaths, of which 29,172 (53%) were men and the rest were women. The overall mortality rate per 100,000 population in men and women was 67.95 and 60.83, respectively. The highest mortality rate in men per 100,000 population was in the age groups above 80 (1497.76), 75-79 (757.35), 70-74 (484.66), and 65-69 (351.78b) years, respectively, and the lowest in the age groups 5-9 (1.15), 10-14 (1.51), 15-19 (2.62), and then 0-4 [3.91], respectively. The highest death rate in women per 100,000 population was in the age groups over 80 (1309.96), 75-79 (781.92), 70-74 (524.30) and 65-69 (318.46) years, respectively, and the lowest was in the age groups 5-9 (0.89), 10-14 (0.92), 15-19 (2.69), and then 20-24 (3.68), respectively. Table 2 shows the mortality rate per 100,000 population by age and sex first year of the study.

The results of the chi-squared test showed that the mortality rates between men and women and years of study were significant differences (p -value < 0.05).

Table 1. Hospitalized and mortality rates per 100,000 population by age and sex first year of study

Male s	Populati on	Death s	Death s per 100,00 0	Hospit a lized	Hospit a lized per 100,00 0	Femal es	Populati on	Death s	Death s per 100,00 0	Hosp it alize d	Hospit a lized per 100,00 0
0-4	3800000	160	4.21	3446	58.58	0-4	3625000	133	3.67	2840	46.84
5-9	3621000	48	1.33	1294	35.74	5-9	3437000	33	0.96	1048	30.49
10-14	3151000	45	1.43	1290	40.94	10-14	3004000	38	1.26	1048	34.89
15-19	2837000	93	3.28	2253	79.41	15-19	2714000	76	2.80	2035	74.98
20-24	2914000	133	4.56	6800	233.36	20-24	2821000	103	3.65	5858	207.66
25-29	3635000	230	6.33	13002	357.69	25-29	3561000	187	5.25	13431	377.17
30-34	4381000	535	12.21	20262	462.50	30-34	4305000	334	7.76	17353	403.09
35-39	4137000	760	18.37	22626	546.92	35-39	4054000	526	12.97	19256	474.99
40-44	3249000	987	30.38	21902	674.12	40-44	3143000	713	22.69	18269	581.26
45-49	2651000	1271	47.94	19931	751.83	45-49	2560000	898	35.08	17333	677.07
50-54	2257000	1870	82.85	21470	951.26	50-54	2214000	1389	62.74	19329	873.04
55-59	1815000	2439	134.38	19970	1100.28	55-59	1827000	1898	103.89	19746	1080.79
60-64	1468000	3668	249.86	22040	1501.36	60-64	1513000	2846	188.10	22192	1466.75
65-69	1001000	4309	430.47	21149	2112.79	65-69	1089000	3468	318.46	21588	1982.37
70-74	620000	4115	663.71	17191	2772.74	70-74	716000	3754	524.30	18659	2606.01
75-79	418000	4126	987.08	14818	3544.98	75-79	448000	3503	781.92	14120	3151.79
80+	530000	10060	1898.11	28765	2708.30	80+	522000	6838	1309.96	20906	2102.30
Total	42485000	34849	82.03	258209	607.77	Total	41553000	26737	64.34	235011	565.57

Table 2. Hospitalized and mortality rates per 100,000 population by age and sex second year of study

Male s	Populati on	Deat hs	Death s 100,00 0	Hospi ta lized	Hospi ta lized per 100,00 0	Femal es	Populati on	Deat hs	Death s 100,00 0	Hospi ta lized	Hospi ta lized per 100,00 0
0-4	3840000	150	3.91	9183	239.14	0-4	3667000	150	4.09	7176	119.36
5-9	3659000	42	1.15	3148	86.03	5-9	3477000	31	0.89	2365	68.02
10-14	3184000	48	1.51	2413	75.79	10-14	3039000	28	0.92	2000	65.81
15-19	2867000	75	2.62	3445	120.16	15-19	2746000	74	2.69	3969	144.54
20-24	2945000	132	4.48	7055	239.56	20-24	2853000	105	3.68	8806	308.66
25-29	3674000	239	6.51	13202	359.34	25-29	3602000	213	5.91	17355	481.82
30-34	4428000	450	10.16	22796	514.81	30-34	4355000	396	9.09	26380	605.74
35-39	4181000	802	19.18	28850	690.03	35-39	4101000	718	17.51	31886	777.52
40-44	3283000	1063	32.38	28794	877.06	40-44	3179000	999	31.42	30821	969.52
45-49	2679000	1288	48.08	25938	968.20	45-49	2589000	1215	46.93	28269	1091.89
50-54	2281000	1786	78.30	26468	1160.37	50-54	2240000	1665	74.33	30567	1364.60
55-59	1834000	2196	119.74	24330	1326.61	55-59	1848000	1966	106.39	29048	1571.86
60-64	1484000	3098	208.76	26928	1814.56	60-64	1531000	2902	189.55	31333	2046.57
65-69	1012000	3560	351.78	24893	2459.7	65-69	1102000	3252	295.10	28045	2544.9

					8						2
70-74	626000	3034	484.66	18180	2904.15	70-74	724000	2994	413.54	21549	2976.38
75-79	422000	3196	757.35	15943	3777.96	75-79	454000	2933	646.04	16634	3663.88
80+	535000	8013	1497.76	30983	2628.41	80+	528000	5927	1122.54	24141	2309.28
Total	42934000	29172	67.95	312549	727.98	Total	42035000	25568	60.83	340344	809.67

4. Discussion

In this study, based on the national population surveillance system data, we compared the hospitalization and mortality rate indexes in total age and sex groups. During the first year, 493220 cases were hospitalized, and 258209 (52%) were men. The overall hospitalized rate per 100,000 population in men and women is 607.77 and 565.57 respectively. During the second year, 652893 cases were hospitalized, and 340344 (52%) were women. The overall hospitalization rate per 100,000 population in men and women was 727.98 and 809.67, respectively. The results of this study showed that hospitalization rate between the two years of study in men and women as not significantly different. Previously, Ithan D. Peltan and colleagues [15] showed the hospitalization rate in women was 43.9%, Joanne Michelle D. Gomez and colleagues showed hospitalization rate in men was higher than women (19% vs. 13%; $p < 0.001$), whilst in our study, sample size was much larger. In the present study, hospitalization rates in age groups was significantly different and higher in older people, which is consistent with study Carla Lourenço Tavares de Andrade [16]. In this study, during the first year of the study, there were 61,586 deaths, where 34,849 (57%) were men. The overall mortality rate per 100,000 population in men and women was 82.03 and 64.34, respectively, whilst in the second year of the study, there were 54,740 deaths, of which 29,172 (53%) were men. The overall mortality rate per 100,000 population in men and women was 67.95 and 60.83, respectively. Results of this study showed that the rate of hospitalization and mortality was different according to age and sex groups. In spite of the strong association between COVID-19 mortality and age and sex, it is critical to contextualize it in relation to other aging-related causes of mortality. There was some variation across countries, where epidemiological data from previous coronavirus epidemics-SARS-CoV (2002) and Middle Eastern respiratory syndrome coronavirus (MERS, 2012) highlighted differences in their manifestation based on sex, with men being consistently more strongly affected than women [17-20]. Publicly available sex-disaggregated data from several governments compiled similar numbers of

COVID-19 cases in men and women, with an increased fatality rate in men as outlined with the male: female ratio of deaths among confirmed cases ranging from 1.0 in Pakistan to 2.1 in Canada, but in a study in India, authors found that the mortality ratio between men and women was non-uniform. The COVID-19 case fatality rate appears to be higher in women than men in a few countries, such as India, which is one of the worst-affected countries. As of Sept 30, 2020, India had more than 6.4 million recorded COVID-19 cases. In India, the COVID-19 case fatality rate among men was 2.9% and 3.3% among women [21]. Regarding the relationship between age and cases of COVID 19, it is evident that older people are more likely to have underlying diseases and a weaker immune system than younger people. The higher risks of death associated with COVID-19 for men may be related to cardiovascular diseases, obesity, diabetes, biological or genetic factors, and the epidemiological profile in each region; but they can also be explained by the deficiencies of the health system [22-24], Hypotheses based on risk factors that are known to change with both sex and age seem to be the most plausible explanations for the differences observed. These include differences in occupation, lifestyle [including smoking and alcohol use], medical comorbidities, or use of medications. These explanations reflect social and cultural factors related to gender rather than the biology of sex. Genetic explanations will need to consider the interaction of age, sex, and risk factors. We urge nations to supply age and sex specific data, not only for an accurate description of the pandemic, but also for the calculation of directly standardized rates, internationally.

Among social factors, it is evident that men represent a higher proportion of smokers, and more often exhibit lifestyles that cause the main comorbidities associated with COVID-19. Moreover, males are more typically reported to engage in cultural practices that put them at greater risk of becoming ill, spreading the infection or seeking less medical attention [8]. The greater susceptibility of men can also be related to their greater amounts of angiotensin-converting enzyme 2 [ACE2] receptors compared to women [9], although further studies are needed to confirm that plasma

ACE2 levels can indicate a higher risk for COVID-19. The lower mortality rates in women might be due to their better immune response regulated by estrogen [25, 26]. Women infected with SARS-CoV-2 have been shown to produce more T cells than men [27]. Likewise, it has been reported that, in the early phase of the disease, women have relatively higher serum concentrations of IgG antibodies against SARS-CoV-2 [28]. According to this study, there were large differences in mortality rate between age groups, where the mortality rate in younger people was very low and higher in older people; this finding is concordant with prior studies [29, 30]. The main limitation of the present study was an underestimation in the number of death cases. Access to the data for this study was difficult, and outpatient data were incomplete so we cannot calculate related indexes.

5. Conclusion

These findings show a higher mortality rate among men than women. In addition, the mortality rate increased with age, and was most predominant in men 50 years of age or older. Our study showed that the burden of COVID-19 is very high and some age groups are more detrimentally impacted, so there is a need for policy makers consider the rate of mortality by age and sex groups and have different, and complementary, strategies for control of pandemic by age and sex groups.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Ethics Committee of the Jiroft University of Medical Sciences (Code IR.JMU.REC.1400.036)

Funding

There was no funding for conducting this study.

Author's contributions

The authors equally contributed to preparing this article. All authors read and approved the final draft of the manuscript.

Conflict of interest

The authors declare that there is no conflict of interest.

Acknowledgments

The authors are pleased to thank the employees of the Disease Management Center of the Ministry of Health of Iran.

References

- [1] World Health Organization. World Health Organization Coronavirus (COVID-19) Dashboard. World Health Organization, Geneva, Switzerland. <https://covid19.who.int>. 2022.
- [2] Rezabeigi-Davarani E, Bokaie S, Mashayekhi V, Sharifi L, Faryabi R, Samakkhah SA, et al. Epidemiological and clinical characteristics of COVID-19 patients studied by Jiroft University of Medical Sciences: southeast of Iran. *J Adv in Med Biomed Res*. 2021;29(136):302-8. [DOI:10.30699/jambs.29.136.302](https://doi.org/10.30699/jambs.29.136.302).
- [3] Navidinia M, Goudarzi M. The main associated symptoms related to covid-19 (Coronavirus disease 2019) among pediatric patients. *Arch Adv Biosci*. 2020;11(3):64-72. [DOI: 10.22037/aab.v11i3.30707](https://doi.org/10.22037/aab.v11i3.30707).
- [4] Xie J, Tong Z, Guan X, Du B, Qiu H. Clinical characteristics of patients who died of coronavirus disease 2019 in China. *JAMA Network Open*. 2020;3(4):e205619-e. [PMID: 32275319](https://pubmed.ncbi.nlm.nih.gov/32275319/) [DOI: 10.1001/jamanetworkopen.2020.5619](https://doi.org/10.1001/jamanetworkopen.2020.5619).
- [5] Dudley JP, Lee NT. Disparities in age-specific morbidity and mortality from SARS-CoV-2 in China and the Republic of Korea. *Clin Infect Dis*. 2020;71(15):863-5. [PMID: 32232322](https://pubmed.ncbi.nlm.nih.gov/32232322/) [DOI: 10.1093/cid/ciaa354](https://doi.org/10.1093/cid/ciaa354).
- [6] Chen T, Wu DI, Chen H, Yan W, Yang D, Chen G, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. *BMJ*. 2020;368. [PMID: 32234718](https://pubmed.ncbi.nlm.nih.gov/32234718/) [DOI: 10.1136/bmj.m1295](https://doi.org/10.1136/bmj.m1295).
- [7] Borghesi A, Zigliani A, Masciullo R, Golemi S, Maculotti P, Farina D, et al. Radiographic severity index in COVID-19 pneumonia: relationship to age and sex in 783 Italian patients. *Radiol Med*. 2020;125(5):461-4. [PMID: 32358691](https://pubmed.ncbi.nlm.nih.gov/32358691/) [DOI: 10.1007/s11547-020-01202-1](https://doi.org/10.1007/s11547-020-01202-1).
- [8] Williamson EJ, Walker AJ, Bhaskaran K, Bacon S, Bates C, Morton CE, et al. Factors associated with COVID-19-related death using OpenSAFELY. *Nature*. 2020;584(7821):430-6. [PMID: 32640463](https://pubmed.ncbi.nlm.nih.gov/32640463/) [DOI: 10.1038/s41586-020-2521-4](https://doi.org/10.1038/s41586-020-2521-4).
- [9] Bhopal SS, Bhopal R. Sex differential in COVID-19 mortality varies markedly by age. *Lancet*. 2020;396(10250):532-3. [PMID: 32798449](https://pubmed.ncbi.nlm.nih.gov/32798449/) [DOI: 10.1016/S0140-6736\(20\)31748-7](https://doi.org/10.1016/S0140-6736(20)31748-7).
- [10] Pradhan A, Olsson P. Sex differences in severity and mortality from COVID-19: are males more vulnerable?. *Biol Sex Differ*. 2020;11(1): 53. [PMID: 32948238](https://pubmed.ncbi.nlm.nih.gov/32948238/) [DOI: 10.1186/s13293-020-00330-7](https://doi.org/10.1186/s13293-020-00330-7).
- [11] Gebhard C, Regitz-Zagrosek V, Neuhauser HK, Morgan R, Klein SL. Impact of sex and gender on COVID-19 outcomes in Europe. *Biol Sex Differ*. 2020;11(1):1-13. [PMID: 32450906](https://pubmed.ncbi.nlm.nih.gov/32450906/) [DOI: 10.1186/s13293-020-00304-9](https://doi.org/10.1186/s13293-020-00304-9).
- [12] Promislow DE .A geroscience perspective on COVID-19 Mortality. *J Gerontol A Biol Sci Ned Sci*.

- 2020;75(9):e30-e3. [PMID: 32300796](#) [DOI: 10.1093/gerona/glaa094](#).
- [13] Austad SN, Fischer KE. Sex differences in lifespan. *Cell Metab.* 2016;23(6):1022-33. [PMID: 27304504](#) [DOI: 10.1016/j.cmet.2016.05.019](#).
- [14] Drzymalla E, Green RF, Knuth M, Khoury MJ, Dotson WD, Gundlapalli A. COVID-19-related health outcomes in people with primary immunodeficiency: A systematic review. *Clin Immunol.* 2022;243:109097. [PMID: 35973637](#) [DOI: 10.1016/j.clim.2022.109097](#).
- [15] Peltan ID, Caldwell E, Admon AJ, Attia EF, Gundel SJ, Mathews KS, et al. Characteristics and outcomes of US patients hospitalized with COVID-19. *Am J Crit Care.* 2022;31(2):146-57. [PMID: 34709373](#) [DOI: 10.4037/ajcc2022549](#).
- [16] de Andrade CLT, Pereira CCdA, Martins M, Lima SML, Portela MC. COVID-19 hospitalizations in Brazil's Unified Health System (SUS). *PLoS One.* 2020;15(12):e0243126. [PMID: 33301479](#) [DOI: 10.1371/journal.pone.0243126](#).
- [17] Karlberg J, Chong D, Lai W. Do men have a higher case fatality rate of severe acute respiratory syndrome than women do?. *Am J epidemiol.* 2004;159(3):229-31. [PMID: 14742282](#) [DOI: 10.1093/aje/kwh056](#).
- [18] Alghamdi IG, Hussain II, Almalki SS, Alghamdi MS, Alghamdi MM, El-Sheemy MA. 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.* 2014;7:417-23. [PMID: 25187734](#) [DOI: 10.2147/IJGM.S67061](#).
- [19] Alwani M, Yassin A, Al-Zoubi RM, Aboumarzouk OM, Nettleship J, Kelly D, et al. Sex- based differences in severity and mortality in COVID- 19. *Rev Med Virol.* 2021;31(6):e2223. [PMID: 33646622](#) [DOI: 10.1002/rmv.2223](#).
- [20] Chen X, Chughtai AA, Dyda A, MacIntyre CR. Comparative epidemiology of Middle East respiratory syndrome coronavirus (MERS-CoV) in Saudi Arabia and South Korea. *Emerg Microbes Infect.* 2017;6(6):e51. [PMID: 28588290](#) [DOI: 10.1038/emi.2017.40](#).
- [21] Joe W, Kumar A, Rajpal S, Mishra US, Subramanian SV. Equal risk, unequal burden? Gender differentials in COVID-19 mortality in India. *J Global Health Sci.* 2020;2(1)e17. [DOI: 10.35500/jghs.2020.2.e17](#).
- [22] Kopel J, Perisetti A, Roghani A, Aziz M, Gajendran M, Goyal H. Racial and gender-based differences in COVID-19. *Front Public Health.* 2020;8:418. [PMID: 32850607](#) [DOI: 10.3389/fpubh.2020.00418](#).
- [23] Abate BB, Kassie AM, Kassaw MW, Aragie TG, Masresha SA. Sex difference in coronavirus disease (COVID-19): a systematic review and meta-analysis. *BMJ Open.* 2020;10(10):e040129. [PMID: 33028563](#) [DOI: 10.1136/bmjopen-2020-040129](#).
- [24] Penna C, Mercurio V, Tocchetti CG, Pagliaro P. Sex- related differences in COVID- 19 lethality. *Br J Pharmacol.* 2020;177(19):4375-85. [PMID: 32698249](#) [DOI: 10.1111/bph.15207](#).
- [25] Fish EN. The X-files in immunity: sex-based differences predispose immune responses. *Nat Rev Immunol.* 2008;8(9):737-44. [PMID: 18728636](#) [DOI: 10.1038/nri2394](#).
- [26] Klein SL, Marriott I, Fish EN. Sex-based differences in immune function and responses to vaccination. *Trans R Soc Trop Med Hyg.* 2015;109(1):9-15. [PMID: 25573105](#) [DOI: 10.1093/trstmh/tru167](#).
- [27] Takahashi T, Ellingson MK, Wong P, Israelow B, Lucas C, Klein J, et al. Sex differences in immune responses that underlie COVID-19 disease outcomes. *Nature.* 2020;588(7837):315-20. [PMID: 32846427](#) [DOI: 10.1038/s41586-020-2700-3](#).
- [28] Zeng F, Dai C, Cai P, Wang J, Xu L, Li J, et al. A comparison study of SARS- CoV- 2 IgG antibody between male and female COVID- 19 patients: a possible reason underlying different outcome between sex. *J Med Virol.* 2020;92(10):2050-4. [PMID: 32383183](#) [DOI: 10.1002/jmv.25989](#).
- [29] Kang S-J, Jung SI. Age-related morbidity and mortality among patients with COVID-19. *Infect Chemother.* 2020;52(2):154. [PMID: 32537961](#) [DOI: 10.3947/ic.2020.52.2.154](#)
- [30] Bonanad C, García-Blas S, Tarazona-Santabalbina F, Sanchis J, Bertomeu-González V, Facila L, et al. The effect of age on mortality in patients with COVID-19: a meta-analysis with 611,583 subjects. *J Am Med Dir Assoc.* 2020;21(7):915-8. [PMID: 32674819](#) [DOI: 10.1016/j.jamda.2020.05.045](#).