



The relationship between demographic indicators and mortality rate of COVID-19 disease comparatively and retrospectively in different waves of COVID-19 disease in Iran

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Abstract

Coronavirus disease-19 (COVID-19) is a novel emerging infectious disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). In this study, we aimed to examine the relationship between demographic indicators and mortality rates in Covid-19 disease in different Covid-19 waves in Iran. In this retrospective cross-sectional study, the study population consisted of 9874 patients of Covid-19 admitted to Hazrat Rasoul Akram Hospital of Tehran, from the beginning of the disease to the end of the fifth wave. Demographic variables such as age and sex as well as clinical variables such as hospitalization date and mortality rate were collected and evaluated. The analysis was performed using SPSS software version 26. The mean age of 9874 participants was 58.9 ± 17.0 years. In this study 5510 (55.8%) of patients were male. 1762 (17.8%) patients died. The fifth wave had the highest number of patients (31.1%) and the trend in the number of patients was increasing from wave second to fifth. However, the percentage of death was lower in waves fourth (14.5%) and fifth (15.3%). The mean age of deceased patients was significantly greater than alive patients (69.25 ± 14.60 vs. 56.76 ± 16.75 , $P=0.0001$). The frequency of male deaths was significantly higher than female deaths ($P=0.0001$). The results of the present study indicate that the frequency of mortality in recent waves, despite a significant increase in hospitalization, has been decreased. It can also be said that mortality increases with age as well as male gender, and males are more prone to death due to covid-19 disease with age.

Keywords: COVID-19, demographic indicators, mortality rate, Iran

1. Introduction

In late December 2019, a novel coronavirus, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) spread in Wuhan, China. The illness caused by SARS-CoV-2 termed coronavirus disease-19 (COVID-19) (1). The COVID-19 was declared a pandemic by World Health Organization (WHO) on 11 March 2020 (2). COVID-19 virus is mostly spread from person to person via respiratory droplet transmission, which happens while a person is in close contact with an infected person. This happens via exposure of the host's mucosal surfaces, including nose, mouth, and eyes to the incoming infective droplets (3, 4). The covid-19 median incubation duration is expected to be 5.1 days, and most of the patients will progress symptoms in 11.5 days of infection (5). 17.9% of covid-19 patients is estimated to remain asymptomatic (6). However, the symptoms of symptomatic patients commonly include fever, cough, as well as shortness of breath. Sore throat, anosmia, nausea, dysgeusia, anorexia, malaise, diarrhea, and

myalgias are reported as less common symptoms (7, 8). RT-PCR was introduced as the standard test for the diagnosis of the virus, however, the importance of chest CT scans in those whose RT-PCR test is false-negative was reported with a sensitivity of 98% (7). Presently, different therapeutic choices are existing for covid-19 including antiviral drugs such as molnupiravir, remdesivir, and paxlovid; anti-SARS-CoV-2 monoclonal antibodies such as bamlanivimab/etesevimab and casirivimab/imdevimab; anti-inflammatory drugs like dexamethasone; and immunomodulators agents such as baricitinib and tocilizumab (9). According to the evidence, older age, suppressed immune systems, presence of underlying cardiovascular, metabolic, and respiratory diseases are risk factors for adverse outcomes (10).

Accurate estimation of epidemiological information, in particular infection and mortality rates, demographic information, and comorbidities, is required to decide on

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epidemic control interventions and regulations (11). In this study, we aim to use the information recorded in the Statistics Center of Rasoul Akram Hospital to examine the relationship between demographic indicators and mortality rate in covid-19 disease in a comparative and retrospective study between different waves of covid-19. The information of this study can be useful in coronavirus management policies and evaluation of the results of vaccination in Iran. So far, no comparative study has been conducted between different waves of Covid-19 in Iran, and with the results of this study, we can examine the difference between the mortality rate of the disease in different waves and the factors affecting the mortality rate of Covid-19 disease in Iran.

2. Materials and Methods

In this retrospective cross-sectional study, a total of 9874 patients were admitted with a definitive diagnosis of Covid-19 disease in Hazrat Rasool Akram Teaching, Research and Treatment Hospital in Tehran, from the beginning of the pandemic to the end of the fifth were included in the study. The sampling method was census.

In order to collect information, after ethical approval, the researcher obtained the list of Covid-19 patients, from the medical records (hospital statistics center unit) of the hospital. The demographic variables such as age and sex as well as clinical variables such as hospitalization date and patient status at discharge (alive and deceased) were collected and evaluated.

In order to determine the disease waves, with the cooperation of the Vice Chancellor for Health of Iran University of Medical Sciences and Health Services, the following dates were determined and announced. The first wave was determined from March 2019 to spring 2020; The second wave was in summer 2020; The third wave was from autumn 2020 and the first half of winter 2021; The fourth wave was from the second half of winter 2021 to spring 2021, and the fifth wave was in summer 2021.

2.1. Statistical analysis

SPSS software version 26 was used for the statistical analysis of data. The results were expressed as mean and standard deviation (mean \pm SD) for quantitative variables and as a percentage for qualitative variables. It should be noted that in

order to investigate the relationship between qualitative variables, Chi-square and Fisher exact tests were used, and also the relationship of quantitative variables, Spearman or Pearson tests were used. In order to measure the relationship between quantitative variables and qualitative variables in parametric conditions, the Student T-test and in non-parametric condition Mann-Whitney U test were used. Paired t-test and its non-parametric equivalent (Wilcoxon) were also used to evaluate quantitative variables before and after the parametric test. A P-value less than 0.05 was considered significant.

2.2. Ethical consideration

The study was performed according to the principles of the Declaration of Helsinki and the ethics committee of Iran University of Medical Sciences (Code of ethics: IR.IUMS.REC.1400.619).

3. Result

The mean age of patients at the time of diagnosis was 58.9 ± 17.0 years. In this study, out of 9874 patients, 5510 (55.8%) were male. Also, 8112 (82.2%) of patients were alive while discharging from the hospital and 1762 (17.8%) died.

The frequency of covid-19 patients in different waves is demonstrated in Table 1. Out of 9874 patients, 3075 (31.1%) were in the fifth wave.

Table 1. The frequency of patients in different waves

Waves	No.	%
First	1453	14.7
Second	1157	11.7
Third	1807	18.3
Fourth	2382	24.1
Fifth	3075	31.1

The mean age of patients and the frequency of different sex and the mortality are shown in Table 2. From the second wave to the fifth wave the mean age of patients was decreased. In all waves, the number of males was higher than females, although from wave third to fifth the number of females increased. Moreover, the percentage of mortality was decreased in waves fourth and fifth.

Table 2. The status of Age, sex, and mortality in patients by disease waves

Waves	Age, mean \pm SD [min, max]	Sex, No. (%)		Mortality, No. (%)	
		Male	Female	Alive	Deceased
First	59.92 \pm 18.27 [10, 98]	877 (60.4)	576 (39.6)	1186 (81.6)	267 (18.4)
Second	61.03 \pm 16.76 [8, 101]	675 (58.3)	482 (41.7)	892 (77.1)	265 (22.9)
Third	60.88 \pm 17.07 [$<$ 1, 100]	1073 (59.4)	734 (40.6)	1391 (77)	416 (23)
Fourth	58.95 \pm 16.88 [3, 98]	1267 (53.2)	1115 (46.8)	2037 (85.5)	345 (14.5)
Fifth	56.69 \pm 16.47 [$<$ 1, 100]	1618 (52.6)	1457 (47.4)	2606 (84.7)	469 (15.3)

The mean age of deceased patients was significantly greater than alive patients. The rate of death was higher in male patients (Table 3).

Table 3. Relationship of age and gender with mortality of patients

	Alive	Deceased	P-value
Age*, mean \pm SD	56.76 \pm 16.75	69.25 \pm 14.60	0.0001
Sex**, No. (%)			0.0001
Male	4445 (45%)	1065 (10.8%)	
Female	3667 (37.1%)	697 (7.1%)	

* t-test, ** Chi-Squared

Table 4 shows that in all waves the mean age was significantly higher in deceased patients.

Table 4. Age status according to mortality in patients in different waves

Waves	Age		P-value
	Alive	Deceased	
First	57.18 \pm 17.96	72.11 \pm 14.22	0.0001
Second	58.92 \pm 16.87	68.11 \pm 14.28	0.0001
Third	57.97 \pm 16.80	70.62 \pm 14.13	0.0001
Fourth	57.05 \pm 16.49	70.13 \pm 14.72	0.0001
Fifth	54.95 \pm 16.13	66.41 \pm 14.84	0.0001

t-test

According to Table 5, the mean age of patients was significantly different between males and females in the first, second, and fourth waves and it was higher in females.

Table 5. Age status according to sex in patients in different waves

Waves	Age, Mean \pm SD		P-value
	Male	Female	
First	58.92 \pm 18.20	61.46 \pm 18.29	0.010
Second	59.98 \pm 16.85	62.50 \pm 16.54	0.011
Third	60.49 \pm 17.53	61.47 \pm 16.38	0.231
Fourth	58.22 \pm 17.15	59.77 \pm 16.54	0.025
Fifth	56.48 \pm 16.72	56.93 \pm 16.18	0.443

t-test

4. Discussion

In this study, the Covid-19 hospitalized cases in Rasoul Akram Hospital in Tehran from the beginning of hospitalization of patients due to Covid-19, March 26, 2019, to the end of the fifth wave of the disease, September 22, 2021, in terms of age, gender, mortality and the relationship between these variables were evaluated.

In a total of 9874 patients, the male population was about 11.6% more than the female population. It should also be noted that the frequency of male deaths was significantly higher than female deaths. The mean age of all patients was 58.9 ± 17 years. Also, the average age of the deceased patients was significantly higher than the alive patients (about 13 years), which indicates that mortality in the covid-19 disease is more likely with older age and the probability of death in older

people are more.

Concerning the frequency of patients in each wave, it can be seen that from the second to the fifth wave, the frequency has increased significantly. Regarding the average age of patients in different waves of the disease, it can be seen that from the first to the second wave, the average age has increased by about a year, and after that, from the second wave to the fifth, the mean age has decreased so that the mean difference of the age of the second to fifth waves is about 4.5 years, which may indicate that newer strains of the virus (such as Delta) cause involvement at younger ages especially in the fourth and fifth waves of the disease. About the gender frequency of people in different waves of the disease, it can be seen that in the first to third waves, the frequency of sexes was close to each other, but in the fourth and fifth waves, compared to the previous three waves, the incidence decreased in males and increased in females.

With regards to the frequency of mortality in different waves, it can be said that the death rate from the first to the third wave is upward and in the fourth and fifth waves, the mortality rate is significantly lower than the previous three waves. Perhaps this obvious and significant decline, despite the fact that the frequency of patients in the fourth and fifth waves was much higher than the previous three waves, can be attributed to the widespread vaccination of the community against this disease.

In a systematic review and meta-analysis by Dessie et al. on 42 studies and 423,117 patients, the results presented that the pooled occurrence of mortality in Covid-19 hospitalized patients was 17.62% (95% CI = 14.26-21.57%). In the current study, 17.8% of patients died as a result of the disease. Similar to the present study, advanced age was increased the mortality risk and the pooled odds ratio and hazard ratio were 2.61(95%CI = 1.75-3.47) and 1.31(95%CI = 1.11-1.51). Also, they found a significant association between Covid-19 mortality and male sex, which is found in this study, with pooled odds ratio and hazard ratio equal to 1.45 (95% CI= 1.41-1.51) and 1.24 (95% CI= 1.07-1.41) (12). In a meta-analysis in Iran by Parohan et al. on publications up to 1 May 2020 (14 studies and 29,909 patients), a significant relation was reported between age older than 65 (pooled OR = 4.59, [95%CI = 2.61-8.04]) and male gender (pooled OR = 1.50, [95%CI = 1.06-2.12]) and the risk of mortality from Covid-19, which is consistent with the result of the present study (13). Alimohammadi et al. study reported that the pooled case fatality rate (CFR) of Covid-19 in hospitalized patients was 13.0% (95% CI= 9.0-17.0) and in patients with age more than 50 years old it was 19.0% (95% CI= 13.0-24.0) (14). In a study in Iran by Nikpouraghdam et al. on 12870 patients from February 2020 to April 2020, most of the cases were in the age range of 50-60 years old. The male to female ratio was 1.93 to 1. The overall CFR was 8.06% among hospitalized Covid-19 patients (15). In another study in southwest of Iran by

Azarbakhsh et al. on 7313 patients with Covid-19 from February to June 2020, 53.5% were male which is close to the result of this study. The CFR was 4.84%. The highest mortality rate was related to patients with different cancers as well as those with age over 80 years (16). Emami et al. assessed the features of patients after the first peak in Fars province in Iran. From the 3702 confirmed covid-19 cases, 87 patients died so the fatality rate was determined 2.35. They also showed that male sex, older age, and comorbidity of diseases particularly diabetes were the main features of deceased patients (17). In the first wave of this study, 18.4% of patients have died. Similar to Emami et al.'s study male sex and older age were associated with mortality. Rahmanian et al. evaluated Covid-19 deceased cases in Jahrom, in the south of Iran, from March to November 2020. 57.54% were men and 42.36% were women. The mean age of the deceased men was 68.7 ± 18.33 and women were 68.82 ± 14.24 years. The result of their study represented that the mortality rate was higher in men than women (18). In Khosravi Shadmani et al.'s study, the epidemiological characteristics of 103,179 Covid-19 patients were evaluated. The average age of men was 52.40 years and females were 52.41 years. 55.2% of the patients were men and 44.8% were women. 60.9% of deaths occurred in the male gender and 39.1% in the female gender and their results were consistent with the result of the current study (19). In Berek et al.'s meta-analysis study on 55 studies and 10014 Covid-19 patients, male patients (OR = 2.41, $P < 0.00001$) and patients with an age of more than 50 years (RR = 3.36, $P = 0.0002$) were affected by SARS-CoV-2 severely (20). According to Zali et al.'s study on 16000 Covid-19 cases from 19 hospitals of Shahid Beheshti University of Medical Sciences, in Tehran, Iran, 1612 patients died. The uppermost rate of death was determined among the age group of more than 65 years as well as intensive care unit (ICU) and critical care unit (CCU) patients. Total CFR was 10.05% and the highest CFR was reported in patients with age higher than 65 years, those with underlying comorbidities as well as ICU/CCU patients (11).

The results of the present study indicate that the percentage of mortality in recent waves of Covid-19 disease, despite a significant increase in hospitalization, has a decreasing trend and the factors affecting this issue can be widespread vaccination in the community, obtaining more experience in treating this disease, presence of more equipment and facilities in identifying and treating the disease, more safety in re-infection of this disease, and starting treatment earlier due to public awareness. The result also shows that mortality increases with age as well as male sex, and males are more prone to death due to this disease with increasing age.

Conflict of interest

There are no conflicts of interest for the present study.

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Authors' contributions

Concept: K.A., A.M., Design: K.A., A.M., Data Collection or Processing: S.S., S.M. Analysis or Interpretation: S.S., S.M. Literature Search: S.S., S.M. Writing: K.A., A.M., S.S.

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