Journal of Medicine in Scientific Research

Manuscript 1010

Subject Area: Internal Medicine

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ORIGINAL STUDY

Comparison of risk factors of mortality during the two coronavirus disease 2019 waves in Delhi, India

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Abstract

Objective: **To determine the risk factors of mortality (in terms of age, sex, and comorbidities) among hospitalized patients in an Indian tertiary care hospital during the first and second waves.**

Patients and methods: **A retrospective observational study was conducted, where the patients' mortality data were collected over two coronavirus disease 2019 (COVID-19) periods, and their characteristics were compared. The first phase was from May 2020 to January 2021 and the second wave was from March 2021 to August 2021.**

Results: **A mortality rate of 23.84% (874 deaths among 3666 patients) and 1.36% (232 deaths among 17 000 patients) was noted in the second and first wave of COVID-19, respectively. Compared with the first wave, second wave deaths had comparable age (65.82 ± 14.82 vs. 67.63 ± 13.78, $P = 0.094$); comparable sex ($P = 0.094$); and significantly lower comorbidities like hypertension (10.18 vs. 27.59%, $P < 0.0001$), diabetes (10.41 vs. 31.47%, $P < 0.0001$), and chronic kidney disease (5.38 vs. 17.67%, $P < 0.0001$). Multivariate regression showed that age, male sex, hypertension, diabetes, and chronic kidney disease were independent significant risk factors of mortality, with adjusted odds ratios of 1.050, 2.754, 2.389, 3.891, and 6.358, respectively, in the first wave, whereas age, male sex, hypertension, and diabetes were independent significant risk factors of mortality (adjusted odds ratio 3.124, 3.412, 5.428, and 6.731, respectively) in the second wave.**

Conclusion: **In comparison with the first wave, the second wave had a higher overall mortality rate and more severe disease even among the patients without significant comorbidities. Higher age and male sex were unanimous significant risk factors of mortality in both the COVID-19 waves.**

Keywords: Coronavirus disease 2019, First wave, Pandemic, Severe acute respiratory syndrome coronavirus 2, Second wave

1. Introduction

The severe acute respiratory syndrome coronavirus 2 causes coronavirus disease 2019 (COVID-19), which evolved into a pandemic, presenting a significant health risk globally. Many nations have seen a two-wave pattern of COVID-19-affected patients, with the first wave occurring in the spring and the second wave occurring in the late summer and autumn [1–4].

In spite of isolated cases being reported in February, the first outbreak of COVID-19 cases in India began in early March 2020 [5]. During the outbreak of first wave, strong prophylactic measures were taken by the Indian government, which included lockdown from March 13th to May 4th and thereafter 3-month duration of progressively increasing social interaction, work, and commercial activities. These measures prevented the early occurrence of the first wave [5].

As of July 2020, life in the country was almost normal, with the requirement of wearing a face mask and maintaining safe social distance. The first wave peaked in September 2020. The world's largest vaccination drive for eligible beneficiaries was

Received 7 March 2022; revised 27 March 2022; accepted 13 April 2022.
Available online 4 March 2024

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https://doi.org/10.59299/2537-0928.1010

initiated on January 16, 2021 [6]. However, an increase in the patients was seen by the end of March 2021 initiating the second wave, which peaked in March 2021. Different parts of the country experienced different stages of the outbreak.

This forced the government to reintroduce strong restrictions, including local and regional lockdowns; shutdown of hotels, restaurants, and cultural and sports events; and a nighttime curfew in containment zones.

Till date of writing the article, that is, February 23, 2022, 42 732 820 patients have been affected by COVID-19, with the rate of mortality being 1.2% ($n = 512\ 924$). The empirical evidence reveals that in terms of age range and disease severity, this second wave differs from the first. As Delhi, India, has a system for reporting death statistics, this study aimed to compare COVID-19 mortality data from the first and second waves in the city, which is one of India's COVID-19 epicenters.

2. Patients and methods

This retrospective observational study was conducted at a Tertiary Care Hospital in Delhi, India. The first phase was from May 2020 to January 2021 and the second wave was from March 2021 to August 2021, during which the data were recorded.

The consent from patients was not required as it was a retrospective observational study. The study did not require ethical approval because there was no intervention.

2.1. Sample size

The study by Iftimie et al. [2] observed that the mortality rate in the first wave was 24% and in the second wave was 13.2%. Taking these values as reference, the minimum required sample size with 80% power of study and 5% level of significance was 200 patients in each study group. The total sample size taken was 1106 (232 in the first wave and 874 in the second wave).

The formula used is as follows:

$$n > = \left(\left(pc^{*}(1-pc) + pe^{*}(1-pe) \right)^{*} (Z_{\alpha} + Z_{\beta})^{2} \right) \Big/ (pc - pe)^{2}$$

with

pc = mortality in first wave.

pe = mortality in second wave.

Where Z_{α} is value of Z at two-sided alpha error of 5% and Z_{β} is value of Z at power of 80%.

The patients' demographic information was acquired. A detailed clinical history of respiratory, cardiovascular, renal, and/or multiorgan dysfunction was recorded. Although the absence of pinpointer history was considered to be nonspecific, only minor symptoms were reported [7]. The gold standard considered for labeling patients as COVID-19 positive was the RT-PCR test. The government's health care system of India plays an important role in offering free RT-PCR testing. In addition, routine laboratory tests performed in all patients were complete hemogram, prothrombin time/international normalized ratio, renal function test, interleukin-6 determination, serum ferritin, and lactate dehydrogenase. Other tests were performed depending on the disease profile of the patients.

The primary outcomes were to find out in-hospital mortality in the first and second waves. The secondary outcomes were to compare the association of age, sex, and comorbidities like hypertension, diabetes mellitus, and chronic kidney disease (CKD) with mortality in the first and second waves. The study flow in shown in Fig. 1.

2.2. Statistical analysis

The data were entered in Microsoft EXCEL and analyzed using SPSS, version 21.0. The data presentation was done as number (%). All qualitative variables, that is, sex and comorbidities were associated using χ^2 test. Independent t test was used to associate age. Univariate and multivariate logistic regression was used to find out significant risk factors of COVID-19 mortality in 2020 and 2021. P value less than 0.05 was considered as statistically significant.

3. Results

A total of 17 000 COVID-19-positive patients were admitted during the first wave, during which 232 (1.36%) patients died. A total of 3666 COVID-19-positive patients were admitted during the second wave, during which 874 (23.84%) patients died (Fig. 2).

Compared with the first wave, the second wave deaths had comparable age (65.82 ± 14.82 vs. 67.63 ± 13.78, $P = 0.094$); comparable sex ($P = 0.094$); and significantly lower hypertension (10.18 vs. 27.59%, $P < 0.0001$), diabetes mellitus (10.41 vs. 31.47%, $P < 0.0001$), and CKD (5.38 vs. 17.67%, $P < 0.0001$) (Table 1).

During the first wave of COVID-19 pandemic, on performing univariate logistic regression, age, sex, hypertension, diabetes mellitus, and CKD were significant risk factors of mortality. With the increase in age, risk of mortality significantly increases, with odds ratio of 1.042 (1.026–1.059). Males and patients with hypertension, diabetes mellitus,

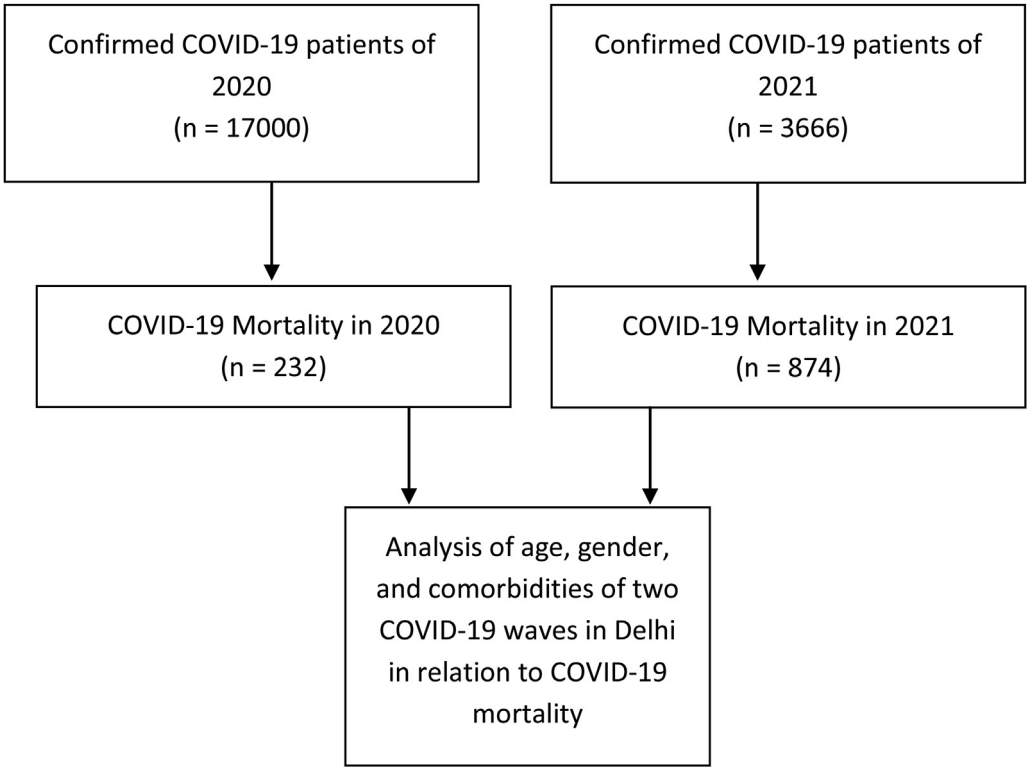

Fig. 1. Study flow diagram.

and CKD had significantly higher risk of mortality with odds ratio of 1.585 (1.185–2.120), 2.214 (1.655–2.961), 2.928 (2.211–3.876), and 6.133 (4.333–8.683), respectively. On performing multivariate logistic regression, age, sex, hypertension, diabetes mellitus, and CKD were independent significant risk factors of mortality. With the increase in age, the risk of mortality significantly increases, with adjusted odds ratio of 1.050 (1.033–1.068). Males and patients with hypertension, diabetes mellitus, and CKD had significantly higher risk of mortality, with adjusted odds ratios of 2.754 (1.579–4.802), 2.389 (1.465–2.982), 3.891 (2.059–5.392), and 6.358 (5.675–10.564), respectively (Table 2).

During the second wave of COVID-19 pandemic, on performing univariate logistic regression, age, sex, hypertension, and diabetes mellitus were significant risk factors of mortality. With the increase in age, the risk of mortality significantly increases, with odds ratio of 3.217 (1.098–4.235). Males and patients with hypertension and diabetes mellitus had significantly higher risk of mortality, with odds ratios of 2.653 (2.013–4.531), 4.576 (2.341–5.638), and 5.672 (3.761–8.913), respectively. On performing multivariate logistic regression, age, sex, hypertension, and diabetes mellitus were independent significant risk factors of mortality. With the increase in age, the risk of mortality significantly increases, with adjusted odds ratio of 3.124 (2.314–3.998). Males and patients with hypertension and diabetes mellitus had significantly higher risk of mortality, with adjusted odds ratios of 3.412 (2.317–5.615), 5.428 (4.761–9.361), and 6.731 (4.516–10.871), respectively (Table 3).

4. Discussion

The COVID-19 pandemic led to a high rate of mortality in the world, demonstrating the severity of the problem. We observed that the mortality rate was higher in the second wave (23.84%) than in the first wave (1.36%). The primary causes of death owing to COVID-19 were acute failure, which included respiratory, renal, cardiovascular, and/or multiorgan involvement [8].

Similar findings were reported in a North Indian study by Budhiraja et al. [9], who observed 40% higher mortality rate in the second wave than the first wave. Consistently, Kumar et al. [10] evaluated data of patients enrolled in the National Clinical Registry for COVID-19 and reported that in the second wave, mortality increased by 3.1%.

In another Indian study, Nath et al. [11] reported that the numbers of deaths in the first wave and second wave were 35 and 65%, respectively, with case fatality rate in the first wave and second wave being 19.2 and 24.18%, respectively.

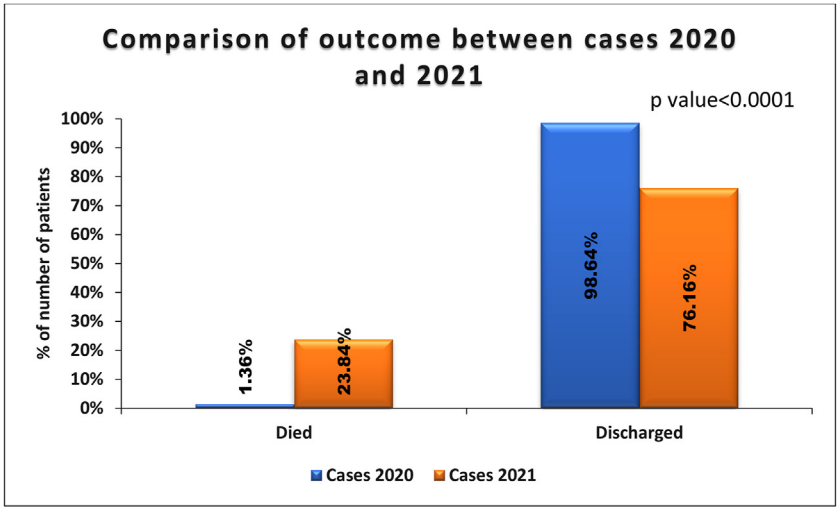

Fig. 2. Comparison of outcome between patient cases in 2020 and 2021.

Jain et al. [12] found that the death rate was not significantly different in the first and second waves; however, because of a higher number of infections, the mortality rate was high. The reason for the non-significance can be the fact that the study was conducted in April when COVID-19 was at the peak.

In a South African study, Jassat et al. [13] also found that in-hospital mortality was higher in the second wave than in the first wave.

On the contrary, Iftimie et al. [2] reported that there were few deaths in the second wave in Spain, although hospital admission rates were higher. The lesser death rates in developed countries could be owing to an advanced health care system. Developed countries were more prepared and experienced when it came to patient treatment. Furthermore, more diagnostic tests were performed, allowing for early identification and successful treatment of serious cases.

Table 1. Comparison of demographic and clinical characteristics between patients who died in 2020 and 2021.

Demographic and clinical characteristics	Mortality 2020 ($N = 232$) [n (%)]	Mortality 2021 ($N = 874$) [n (%)]	P value
Sex			
Female	64 (27.59)	262 (29.98)	0.478[a]
Male	168 (72.41)	612 (70.02)	
Age (years)	67.63 ± 13.78	65.82 ± 14.82	0.094[b]
Comorbidities			
HTN	64 (27.59)	89 (10.18)	<0.0001[b]
DM	73 (31.47)	91 (10.41)	<0.0001[b]
CKD	41 (17.67)	47 (5.38)	<0.0001[b]

CKD, chronic kidney disease; DM, diabetes mellitus; HTN, hypertension.

[a] Independent t test.

[b] χ^2 test.

The higher number of cases in India's second wave could be owing to many factors. The mutant virus was discovered to have a higher transmission potential and a shorter incubation period. The public demonstrated reluctance for 'COVID-Appropriate Behaviors,' or CAB, and the masks utilized varied greatly in quality. N-95 masks are not frequently utilized in India due to their greater costs, and the majority of the patients preferred to use either local cotton masks or the same old worn-out masks [14].

The high increase in the number of affected cases could be attributed to increased testing. However, there are concerns about the quality of testing, because several patients with symptoms of COVID-19 were found to have negative RT-PCR test results [11–14].

We observed that age and sex of patients who died in the second wave were similar as that of the first wave deaths. Overall, elderly individuals were affected more by COVID-19. Moreover, there were more male patients in both the waves. The age, sex, hypertension, diabetes mellitus, and CKD were independent significant risk factors of mortality in both waves, whereas CKD was only an additional risk factor of mortality in the first wave.

The presence of comorbid metabolic conditions such as diabetes mellitus, hypertension, and CKD weakens immunity, resulting in greater susceptibility and disease severity, reduced clearance of airway and mucus, restrictions of medicine treatment, and cross–drug interactions, which are linked to an increased risk of infection and death in the elderly [10].

Treatment preference is not given at the onset of disease symptoms to nonearning, dependent elderly

Table 2. Univariate and multivariate logistic regression to find out significant risk factors of coronavirus disease mortality in 2020.

Variables	Univariate		Multivariate	
	P value	Odds ratio	*P* value	Adjusted odds ratio
Age (years)	<0.0001	1.042 (1.026–1.059)	<0.0001	1.050 (1.033–1.068)
Sex				
Female	Reference			
Male	0.002	1.585 (1.185–2.120)	0.0004	2.754 (1.579–4.802)
Hypertension	<0.0001	2.214 (1.655–2.961)	<0.0001	2.389 (1.465–2.982)
DM	<0.0001	2.928 (2.211–3.876)	<0.0001	3.891 (2.059–5.392)
CKD	<0.0001	6.133 (4.333–8.683)	<0.0001	6.358 (5.675–10.564)

CKD, chronic kidney disease; DM, diabetes mellitus.

in developing countries, usually because of family financial constraints. This causes symptoms to worsen, and the disease may progress to systemic, irreversible complications before people seeking medical treatment [8].

Males have a higher risk of infection and death because of more outside exposure because they are still the family's primary earner, implying more exposure of social gathering, longer travel stretches, and weakened immunity related to smoking and alcohol consumption [8].

This is in accordance with the findings by Nath et al. [11], as age and sex were similar in both groups. Similarly, Budhiraja et al. [9] found that age was comparable in both waves; however, females were admitted slightly more in second wave.

However, Kumar et al. [10] found that among the deceased patients in the second wave, there was an increased mortality among all age groups with the exception of those under the age of 20 years, where mortality declined. There were lesser number of males in the second wave (63.7 vs. 65.4%, $P = 0.02$).

Iftimie et al. [2] reported that patients of the second wave were younger than those of the first wave. Other previous studies from different countries found similar findings [3,4,15]. The reason for the difference in the two waves is still not known.

Aleta and Moreno [16] and Fan et al. [3] reported that there was more infection in young, healthy adults, and children, which could be due to reluctance of young age individuals to follow norms of social distancing.

We found that nonsurvivors in second wave deaths had significantly lesser cases of hypertension, diabetes mellitus, and CKD.

Similarly, Kumar et al. [10] reported that the second wave non-survivorss had significantly less number of comorbidities. However, in another Indian study [9], second wave cases were found to have significantly more comorbidities such as diabetes or hypertension (59.7 vs. 54.8%, $P < 0.001$).

However, concomitant diseases were comparable in both waves in the study by Iftimie et al. [2], which was similar to another study by Iftimie et al. [17]. In contrast, Saito et al. [4] reported cerebrovascular and cardiovascular diseases to be present in a lesser number of COVID-19 patients in Japan. Di Castelnuovo et al. [18] reported that impaired renal function, but not obesity, CVD, or cancer, and advanced age were the main predictors of in-hospital mortality.

These chronic illnesses have also been identified by the WHO as the greatest cause of death [19]. In the case of diabetes mellitus, persistently high blood sugar levels weaken the immune system, making it more susceptible to infection. Although there is no established mechanism for diabetes related to COVID-19 severity, the possibility of angiotensin-converting enzyme 2 (ACE2) overexpression in diabetes mellitus has been suggested.

COVID-19-infected patients are reported to have the highest rate of hypertension of any cardiovascular disorders. The exact mechanism of myocardial damage in COVID-19-infected patients is unknown; however, it is possible that the virus causes

Table 3. Univariate and multivariate logistic regression to find out significant risk factors of coronavirus disease mortality in 2021.

Variables	Univariate		Multivariate	
	P value	Odds ratio	*P* value	Adjusted odds ratio
Age (years)	<0.0001	3.217 (1.098–4.235)	<0.0001	3.124 (2.314–3.998)
Sex				
Female	Reference			
Male	0.0003	2.653 (2.013–4.531)	0.0009	3.412 (2.317–5.615)
Hypertension	<0.0001	4.576 (2.341–5.638)	<0.0001	5.428 (4.761–9.361)
DM	<0.0001	5.672 (3.761–8.913)	<0.0001	6.731 (4.516–10.871)
CKD	0.059	2.133 (0.081–4.512)		

CKD, chronic kidney disease; DM, diabetes mellitus.

myocarditis and pericarditis, which lead to arrhythmias as well as heart failure; increased ACE2 expression, which causes damage to cardiac tissue, and acute cardiac injury, which leads to cardiac failure. In the presence of hypertension, additional pressure is placed on cardiac muscle pumps, resulting in cardiac collapse. Although the specific mechanism by which the COVID-19 virus affects renal tissue is unknown, the kidney's expression of ACE2 may play a major role [8].

COVID-19-related mortality was more common in elderly males with comorbidities. Thus, the immunization campaign was being prioritized to reach the high-risk population first. To combat the pandemic in the future, this vulnerable group should exercise extreme vigilance, and vaccination programs should be accelerated to reach nearly 70% of the population. Future research is needed to improve diabetes treatment and find new approaches to manage patients through technological advancements like telecare [8].

4.1. Limitations

One of the limitations was that research was limited to a single center and particular geographic area; thus, its findings cannot be generalized. However, the study's findings are important because they could represent patients in India and other developing nations, about which there is currently little information.

4.2. Conclusion

To sum up, the second wave had higher overall mortality and severe disease than the first wave; however, it afflicted a demographic population that was similar in age and sex in comparison to the first wave. Higher age, male sex, and presence of comorbidities like hypertension and diabetes hold a significantly higher risk in COVID-19 mortality, and thus, it demands a watchful monitoring of such patients.

Conflicts of interest

There are no conflicts of interest.

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