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Original Research Article

Mortality analysis in cases of COVID-19 during the second wave at a tertiary care center in western India

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ABSTRACT

India witnessed a devastating second surge of COVID-19 cases from March 2021. Evidence strongly advocates its association with the patients' age, gender, pre-existing comorbidity, vaccination status, and Remdesivir administration during the treatment of the disease. The objective of this study is to evaluate the significant relation of these five factors to in-hospital COVID-19 mortalities. We conducted a retrospective, cross-sectional, and observational cohort study between Jan 01 and May 30, 2021 in a tertiary care center in India. The outcome of interest is to identify the effect of vaccination, co-morbidities, and Remdesivir administration on COVID-19 mortality using SPSS software version 25.0 (IBM Corp., Armonk, NY, USA). The mortality rate was found to be 6.8 % (N=117) during hospitalization. The mean age of patients who died due to COVID-19 was 70.41 ± 15.04 years and the median was 68.34 (IQR: 59.61-83.38) years. About 89% of the population was over 55 years of age. The mortality rate was found to be higher in males (N=77; 65.8%). Out of 117 deaths, 95 patients (81.2%) were unvaccinated, whereas only 15.4% (N=18) and 3.4% (N=4) have taken a single and double dose respectively. Approximately, 3 quarter of patients had 1 or more comorbidity. Remdesivir administration is associated with the survival of 84.0% in moderate to severe COVID-19 infected patients. Results of our study coincide with the outcomes of studies done in the past concluding that age, gender, pre-existing comorbidities, vaccination status, and Remdesivir administration, these five factors are associated with COVID-19 mortalities.

1. Introduction

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) induced coronavirus disease 2019 (COVID-19) has spread on an unprecedented scale, resulting in a global pandemic. Like several parts of the world, India experienced the second wave of COVID-19 from March 2021, which lead to a severe crisis in the form of spiralling cases, shortage of essential supplies and treatments, and increased deaths.[1] Second wave has created more havoc in India, by contributing to almost 47% of single-day incident cases in the world during its peak and intensifying the social and economic devastation.[2] As of November 21, 2021, India is the 2nd leading country in the absolute number of cumulative COVID-19 cases with a record of 34.5 million infections and 4,65,000 reported deaths.[3]

Patients affected in the first wave of COVID 19 were mostly elderly populations greater than 60 years of age. However, in the second wave, the younger adults appear to be more prone to COVID 19 and their vulnerability to the infection was not apparent and beyond any scientific explanations. The associated symptoms of COVID 19 and the ability to sustain and recover from infection were variable among the patients.[4–6] During the second wave, the mortality rate increased up to 40 % in India, where the younger population aged < 45 years is mostly affected.[5] Patient age, gender, and comorbidities are considered to be one of the important

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factors for hospitalization and mortality.[7,8] Evidence has clearly demonstrated that individuals with pre-existing comorbidities such as hypertension, cardiovascular disease, and diabetes are at a much greater risk of dying from COVID-19. This is of great concern for individuals living with these conditions, given that comorbidities are associated with high mortality among COVID-19.[9,10]

The spectrum of COVID-19 infection ranges from asymptomatic to extremely severe cases. Many infected people would experience mild to moderate symptoms and recover without medical intervention.[11,12] However, in some cases, the infection was prone to life-threatening illness requiring special medical care among COVID 19 patients. It is reported that COVID-19 mRNA vaccines provide 95 % protection among the symptomatic patients, though transmission risk from asymptomatic cases remains a matter of concern.[13] In addition, administration of remdesivir in patients with severe COVID-19 treated over a course of 10-days has shown to reduce recovery time significantly than those receiving placebo (11 days vs 15 days).[14] Concurrent with this evidence, we sought to determine the fatality rate at our tertiary care center during the second wave of the COVID-19 pandemic in India. The aim of our study is to evaluate how age, gender, pre-existing comorbidities, effect of vaccination, and remdesivir administration adversely affect COVID-19 mortality.

2. Materials and Methods

2.1. Study design

A retrospective, cross-sectional, and observational cohort study was conducted to evaluate the risk factors associated with in-hospital mortality due to COVID-19 during second wave at a tertiary care center in a metropolitan city of western India. All patients aged above 40 years admitted to hospital with confirmed COVID-19 from 01 Jan 2021 till 30 May 2021 were included in the study. The study end-point was to identify the effect of vaccination, co-morbidities, and Remdesivir administration on mortality. The informed consent was obtained for each participant.

Confirmed COVID-19 was defined as a positive real-time reverse transcriptase–polymerase chain reaction (RT-PCR) or rapid antigen test (RAT) for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in a respiratory sample at any time during or before admission. Repeated testing was performed when there was a high clinical suspicion, but negative initial testing. The severity of illness was defined as per the national guidelines issued by the Indian Council of Medical Education and Research (ICMR) to include mild, moderate, and severe cases.[15]

2.2. Data source and extraction

From the electronic medical records, the data were collected as per designed proforma including patient characteristics, comorbidities, clinical symptoms, number of doses of vaccination, the severity of illness, progression of severity, and days of hospitalization. Parameters were selected based on clinical relevance and study objective.

2.3. Study variables

The demographic characteristics examined included age, gender, and vaccination status.

2.4. Clinical characteristics

Clinical characteristics included baseline comorbidities.

2.5. Pharmacological therapy

Remdesivir administration status was evaluated to check its effect on mortality.

2.6. Clinical outcome

Clinical outcomes assessed included in-hospital mortality and total hospital length of stay (LOS). In-hospital mortality was defined as the percentage of patients with COVID-19 who died in the hospital.

3. Statistical Analysis

The statistical analysis was done using SPSS software version 25.0 (IBM Corp., Armonk, NY, USA) and Microsoft Corporation. (2019), Microsoft Excel. The continuous variables were expressed as mean + standard deviation (SD) or median (Intra-quartile ranges) and categorical data were expressed in the form of numbers and percentages. Categorical variables were compared using the chi-square test. Fisher's exact test was employed instead of the chi-square test when > 20% of the cells had expected frequencies <5. For analysis, a two-tailed P-value of <0.05 was considered statistically significant.

4. Results

During the second wave of COVID-19, 1714 laboratory-confirmed cases of COVID-19 were admitted between 01 Jan 2021 and 30 May 2021 in a tertiary care centre, of which 117 patients succumbed to death (Figure 1). The mortality rate was found to be 6.8 % (N=117) during hospitalization. The data of these patients were used for further analysis to serve the purpose of this study i.e., to identify the effect of vaccination, co-morbidities, and Remdesivir administration on mortality.

4.1. Demographic profile of patients who were hospitalized and died due to COVID-19

Demographic characteristics analysed in this study population were age, gender, and vaccination status. The

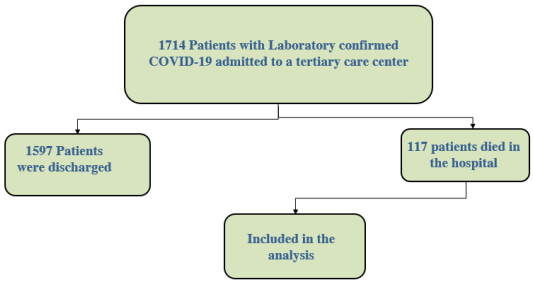

Fig. 1: Flowchart of cohort

mean age of patients who died due to COVID-19 in this tertiary care center was 70.41 ± 15.04 years and the median was 68.34 (IQR: 59.61-83.38) years. About 89% of the population was elderly over 55 years old. The patients who died due to COVID-19 were predominantly male (N=77; 65.8%). The cases were mostly severe in nature (82.1%) and the majority of patients were not vaccinated. Out of 117 deaths, 95 patients (81.2%) had not taken any COVID-19 vaccination, whereas only 15.4% (N=18) and 3.4% (N=4) were administered with single and double doses respectively (Table 1).

Table 1: Demographic characteristics of patients who were hospitalized and died due to COVID-19

Characteristics (N=117)	Category	N (%)
Gender	Male	77 (65.8%)
	Female	40 (34.2%)
Age	≤40	0 (0%)
	41-55	13 (11.1%)
	56-70	54 (46.2%)
	≥71	50 (42.7%)-
Vaccination Status	None	95 (81.2%)
	One	18 (15.4%)
	Both	4 (3.4%)
Severity Status	Mild	0 (0%)
	Moderate	21 (17.9%)
	Severe	96 (82.1%)

Overall, the hospitalized patients with COVID-19 showed that the vaccination status and severity had a significant effect on the mortality of COVID-19 patients ($p < 0.0001$) (Table 2). 99.2 % of patients with complete vaccination were alive while 0.8% of patients died (Figure 2). All the patients with mild COVID-19 were alive and discharged from the hospital while 93.8% of patients with moderate COVID-19 survived and 6.3% of patients died. More than half of severe cases (54.5%) couldn't survive COVID-19.

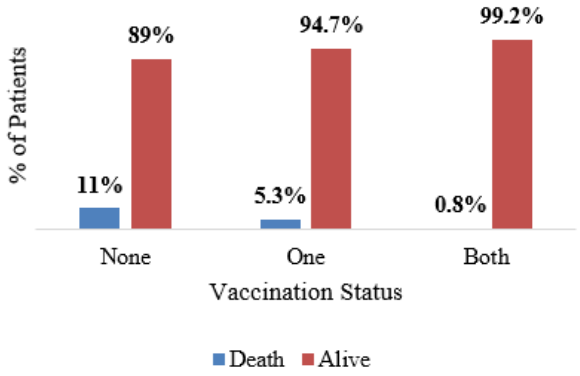

Fig. 2: Vaccination status and its association with mortality

4.2. Effect of severity of COVID-19 and vaccination status on mortality

The hospitalized patients who died due to COVID-19 with no vaccination or with one dose of vaccine were mostly due to the severe nature of the disease (82.1% and 83.3% respectively) and followed by moderate COVID-19 (17.9% and 16.7 respectively) while patients with both doses of vaccine died 75% when the disease was severe and only 25% when disease in moderate. It can be concluded from the analysis that there was a significant relationship between the severity of COVID-19 and vaccination status ($Chi^2 = 391.20$; $p<0.0001$) (Table 3).

4.3. Baseline comorbidities

Around half of the population was suffering from hypertension (48.7%), while diabetes mellitus (41.9%) was the second most common comorbidity in the COVID-19 patients who couldn't survive this disease (Table 4). Approximately 3 quarter of patients had 1 or more comorbidity (Figure 3).

4.4. Effect of pharmacological therapies

Remdesivir was given along with steroids to 238 COVID-19 patients who had moderate to severe infection at the time of hospital admission. Out of those only 38 (16%) patients had mortality. On the other hand, 79 (37.6%) patients who had moderate to severe COVID-19 infection where remdesivir was not administered experienced mortality. So, its administration appeared to have survival benefits among patients ($Chi^2 = 27.11$; $p < 0.0001$). Remdesivir

Table 2: Overall vaccination status and severity of COVID-19 among both alive and dead patients.

Characteristics (N=1714)		**Mortality Status among hospitalized**			
		Death	Alive	Total	Chi-Square,P-value
Vaccination Status	None	95 (11.0%)	766 (89.0%)	861	
	One	18 (5.3%)	324 (94.7%)	342	Chi^2= 54.62 p <0.0001
	Both	4 (0.8%)	507 (99.2%)	511	
	Total	117 (6.8%)	1597 (93.2%)	1714	
Severity at the time of admission	Mild	0 (0%)	1202 (100%)	1202	
	Moderate	21 (6.3%)	315 (93.8%)	336	Chi^2= 710.60p <0.0001
	Severe	96 (54.5%)	80 (45.5%)	176	
	Total	117 (6.8%)	1597 (93.2%)	1714	

Table 3: The effect of both vaccination status and severity on mortality of patients due to COVID-19

Characteristics (N=117)		**Covid-19 Severity at the time of hospital admission**				
		Mild	Moderate	Severe	Total	Chi-Square, P value
Vaccination Status	None	0 (0%)	17 (17.9%)	78 (82.1%)	95	
	One	0 (0%)	3 (16.7%)	15 (83.3%)	18	Chi^2= 391.20 P <0.0001
	Both	0 (0%)	1 (25%)	3 (75%)	4	
	Total	0 (0%)	21 (17.9%)	96 (82.1%)	117	

Table 4: Comorbidities among patients who were hospitalized and died due to COVID-19.

Comorbidities	N (%)
Hypertension	57 (48.7%)
Diabetes Mellitus	49 (41.9%)
Hypothyroidism	11 (9.4%)
Cardiac	18 (15.4%)
Respiratory	7 (6%)
Other	19 (16.2%)

Table 5: The length of stay of patients who died due to COVID-19.

Characteristics (N=117)	**Category**	**N (%)**
Length of stay (In Days)	≤3	33 (28.2%)
	4 to 6	29 (24.8%)
	7 to 9	19 (16.2%)
	10 to 12	16 (13.7%)
	13 to 15	8 (6.8%)
	≥16	12 (10.3%)

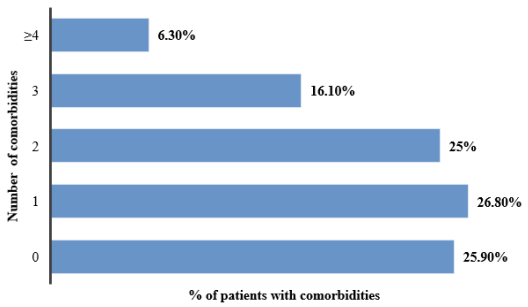

Fig. 3: Graph of the number of patients against the number of comorbidities.

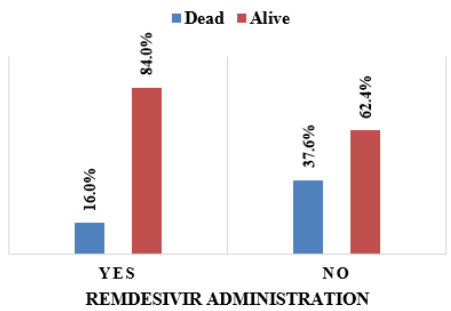

Fig. 4: Remdesivir administration status among patients with COVID-19.

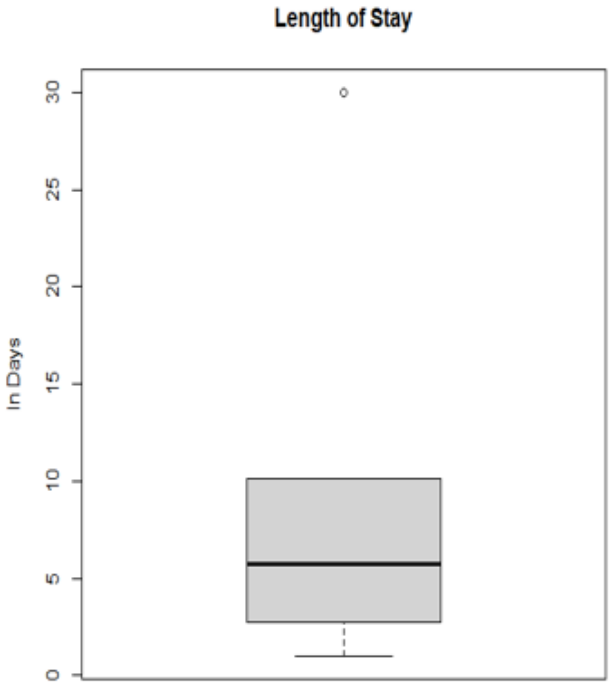

Fig. 5: Length of stay for deceased COVID-19 patient.

administration seemed to have a beneficial effect leading to the survival of 200 (84.0%) patients with COVID-19 as compared to the non-remdesivir group (131, 62.4%) (Figure 4).

4.5. Total Hospital length of stay

As shown in Table 5, approximately more than half (53.0%) of patients died within 6 days of hospitalization (28.2% (n=33) died within ≤3 days from admission, whereas 24.8% (n=29) had died between 4 to 6 days). The mean length of stay was reported as 7.78 ± 6.42 days while the median length of the stay was 6.13 (IQR: 2.70 – 10.2) days (Figure 5).

5. Discussion

Since the emergence of COVID-19, much data has been published stating that the increased age, gender, and any pre-existing comorbidity pose an adverse effect on the prognosis of the disease, thereby increasing its mortality rate. In this study, we found that increased age (>55 years), male gender, and presence of comorbidities affected the disease adversely leading to severe symptoms and death. Fang H et al. in their study found most of the severally and critically ill COVID-19 patients were males, while higher age and presence of comorbidities are significantly associated with increased mortality rate.[16] Biswas M et al. found similar results demonstrating a higher mortality rate among males than females ($p < 0.00001$), and a 15.4-fold greater rate of mortality among older patients ($p < 0.00001$).[17] Results of the study by Surendra H et al. again coincide with our findings showing an increased mortality rate in males (14% vs 10%), older patients (median 58 vs 44 years), and patients with a history of comorbidity (62% vs 27%).[18] Vila-Corcoles et al. found that as per age, case-fatality was 1.7% in 50–64 years, 25.5% in 65–79 years, and 38.7% in 80 years or older ($p < 0.001$) supporting the results of our study suggesting increased age, male predominance ($p < 0.001$), and the existence of comorbidities is related to COVID-19 mortality.[19] In a study comparing the epidemiological data from the first and the second wave of COVID-19, Sarkar A et al. in their study reported that the most affected age groups were 11–30 years, 31–45 years, and 46–60 years, followed by 61–80 years, 81–100 years and 1–10 years. Additionally, India and the rest of Asia registered a higher number of mortalities among males in both the first wave (male patients: Asia, 61.4%, India, 64.9%) and the second wave (male patients: Asia, 59.54%, India, 71.09%).[20] In an analysis of the first and second waves of the pandemic, Bogam P et al. reported 7920 deaths among the 465,192 confirmed cases with a mortality rate of 1.7% in the cohort. Of the deceased patients, the median age was found to be 65 years, and 47% of patients had at least one or more underlying comorbidities.[21] Our findings are compatible with these studies.

In this study, administration of Remdesivir may be associated with survival in the COVID-19 population. Alike results were obtained by Flisiak R et al. who reported the higher discharge rate of patients from the hospital on days 21 and 28 among patients receiving Remdesivir with higher demonstrated rates of clinical improvement compared to patients treated with other medicines.[22] In correspondence to our results Garcia-Vida C et al. conclude that Remdesivir is an effective drug in lowering the COVID-19 mortality rate along with a good safety profile.[23]

In our present study, vaccination against COVID-19 is found to be effective in lowering the severity of the disease and thereby reducing the death rate. Based on real-life public data, Jabłonska K et al. confirm the effectiveness of vaccination against COVID-19 mortalities to be very strong, providing around 72% protection from death.[24] Victora CG et al, in their study, found a tremendous decline in mortality rate among elderly people due to the early impact of vaccination against COVID-19. Authors revealed that an estimated additional 43,802 COVID-related deaths were predicted in due course of time, if no vaccination was provided, thus substantiating the accuracy of the results of our study.[25] Similar outcome was experienced by Macchia A et al. who evaluated a COVID-19 vaccine campaign and mortality among adults 60 years of age and more, suggesting a significant reduction in documented COVID-19 infection and associated mortalities.[26] Pritchard et al. found that the vaccination against COVID-19 was

extremely aiding in reducing the incidence of new infection in the overall population.[27] According to a meta-analysis study by Liu et al., vaccination against COVID-19 is highly effective in lowering the rate of death, severe and symptomatic cases, and infections.[28] Shah ASV et al. provided empirical evidence showing that vaccination was helpful in lowering the COVID-19 infection burden on the members of the household of healthcare workers concluding that vaccination is the most direct way to curtail the spread of the deadly disease.[29]

The present study has a limitation of being single-centered with a lower number of patients included. Further studies must be performed on a larger scale to substantiate the results with more real-life evidence, and conformity.

6. Conclusion

The present study suggests that increasing age, male gender, and one or more pre-existing comorbidity poses an adverse effect on COVID-19 prognosis, thereby increasing the COVID-19 mortality rate. Vaccination has a positive outcome on the disease and is associated with a reduced COVID-19 mortality rate during the second wave. Remdesivir administration conferred a modest mortality benefit in our cohort and may be associated with improved survival in moderate to severe COVID-19 patients. It is imperative to continue investigating the optimal supportive care measures to enhance further clinical outcomes during the following waves among moderate to severe COVID-19 patients.

7. Source of Funding

None.

8. Conflict of Interest

None.

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