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Original Research Article

Predictors of mortality among COVID-19 patients admitted in a dedicated COVID hospital during the pandemic in Himachal Pradesh, India

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ABSTRACT

Background: The outcome of COVID-19 disease is variable. Mostly patients have mild to moderate disease and get recovered; some patients have severe disease leading to mortality. Hence it is essential to find out the factors affecting the outcome in the COVID-19 patients. The aim of this study was to identify predictors of mortality among hospitalized patients of COVID-19 and to estimate their prevalence among these patients.
Methods: This was an observational study, longitudinal in design, carried out among 790 COVID-19 patients hospitalized in a tertiary care dedicated COVID hospital in Himachal, during the second wave of COVID.
Results: Overall 26.2% of the hospitalized patients were having one or more co morbidities. DM (17.6%) and delayed hospitalization (42.7%) were highly prevalent risk factors among hospitalized patients with high mortality 39.6% and 49% respectively. Overall mortality rate among study participants was 29.7%. Patients having malignancy and other immuno-compromising diseases had highest mortality rate 68.4%. Median time gap between onset of symptoms and hospitalization was 9 days among those who died and 5 days among those who recovered. On multivariate logistic regression analysis higher age (>60 years) AOR 5.392 (3.435-8.463), delayed hospital admission AOR 8.204 (5.522-12.188), diabetes mellitus AOR 1.888 (CI-1.199-2.972), malignancy and other immune compromising diseases AOR 9.108 (2.934-28.270) and chronic kidney disease AOR 7.524 (CI=2.289-27.735) were the significant predictors of mortality.
Conclusions: We observed the higher COVID-19 mortality among the patients having higher age, DM, CKD, immunocompromising diseases and delay in hospitalization. DM and delayed hospitalization were two most prevalent risk factors present among these patients.

Keywords: COVID-19 mortality, Comorbidities, Pandemic, Predictors, Delayed hospitalization

INTRODUCTION

The World Health Organization (WHO) declared corona virus disease 2019 (COVID-19) as pandemic on 11 March 2020. By May 2021, more than 185 million cases of COVID-19 disease had been reported throughout the world. In India, the first case was documented on 30th January 2020 in Kerala.[1] The number of COVID-19 patients increased in the next few months reaching 96000 cases per day by September 2020 and then there was decline in the number of COVID-19 cases which reached at 9000 cases per day by February 2021, but at the end of March 2021 the number of cases started rising again known as second wave of COVID pandemic in India. By 30th May, 2021, more than 2 million confrmed cases had been reported in India.[2]

Majority of the individuals who get infected with novel corona virus (COVID-19 virus) remain asymptomatic or have mild to moderate disease but in few patients the diseases progress so fast that the patient dies within a few days. It could be concluded that the outcome of COVID-19 depends on various epidemiological factors which need to be explored to find out the predictors of mortality.

Various studies from different countries of the world have documented mortality rate ranging from 1.6% to 61.5%, depending on the patient's age and comorbidity profile.[3,4] Comorbidities have been found to have significant role to play. Few studies have also reported: delay in hospital admission predicts the mortality in COVID-19 patients.[5,6] It is important to study all the factors which might affect the mortality in COVID-19 patients. The results can be used for planning the early interventional strategies both at community level and hospital level, to reduce the mortality. With this background we planned to study the predicting factors of mortality among hospitalized COVID-19 patients.

METHODS

Shri Lal Bahadur Shastri Government Medical College Mandi at Ner chowk is a tertiary care hospital in Himachal Pradesh which was designated as dedicated COVID hospital for treatment of COVID-19 patients in Himachal during the COVID-19 pandemic. During second wave of COVID-19 in India, this centre started admitting the patients from 21st April 2021 onwards. The current study was an observational prospective cohort study including all COVID-19 patients who were admitted to this centre between 21 April and 30 May 2021 (the study period) and were fulfilling the inclusion criteria.

Inclusion criteria

All patients who were RT-PCR or RAT positive for COVID-19 and having SpO_2 level <94% were included in the study.

Exclusion criteria

Patients who were discharged on request before recovery and who were referred to higher institute were excluded from study.

The data was collected both by interviewing patients or attendants and from the patient records available in the wards on a predesigned proforma after taking informed consent. Outcome was recorded after patient had either died or recovered and discharged. The study was approved by the institutional ethics committee. The variables studied were: age, gender, comorbidities (diabetes, hypertension, CAD, CKD, malignancy and other immunosuppressive diseases) and delay in hospital admission. Delay in admission was considered to be present when the time gap between onset of symptoms and hospitalization was of more than 7 days.

All statistical analysis were performed by using data analyzing software IBM statistics statistical package for the social sciences (SPSS) (version 22). Both descriptive and logistic regression analysis were performed. All variables were examined to compare differences between dead and discharged patients by Chi-square test. A univariate logistic regression analysis was done for each variable and OR was obtained. After that all the significant variables were entered into multivariate logistic regression analysis model and the adjusted odds ratios (AOR), with minimum 95% confidence intervals (CI), were obtained for them. The adjusted odds ratios were the independent OR for each variable, controlling for all other variables entered into the multivariate logistic regression analysis. Statistical significance was considered when p value was less than 0.05 for all statistics.

RESULTS

Total 832 patients were admitted in this hospital during the study period, out of which 42 patients were either referred to higher institutes or discharged on request before recovery hence excluded from study analysis. Finally, 790 patients were included in the analysis. Overall, 26.2% of the hospitalized patients had comorbidities, 7% patients were having HTN, 17.6% had DM, 1.9% had CKD, 1.4% CAD, 2.5% were having malignancy or other immuno-compromising diseases. Overall, 337 (42.7%) patients were having delayed hospital admission i.e., admitted to hospital after 7 days of onset of symptoms) (Table 1).

Total 235 (29.7%) patients died and 555 (70.3%) patients were discharged after recovery. The mean age of study participants was 52.2 years (SD-17.3 years). The mean age of patients who died was 58.9 years (SD-14.9 years) and mean age of patients who survived was 49.4 (SD-17.6 years). 70.2% of patients who died, and 30.9% of the recovered and discharged patients, were admitted to the hospital after 7 days of onset of symptoms. Over all median time gap between onset of symptoms and hospitalization was 7 days (IQR 4-9 days). It was 5 days (IQR 3-8 days) among patients who recovered and 9 days (IQR 7-11 days) among the patients who died.

Among the highly prevalent variables (HTN, DM, delay in hospitalisation) mortality was highest 49% in the patients with delayed hospitalization. Among the less prevalent variables (CAD, CKD, malignancy and other immunocompromising diseases) patient having malignancy and other immuno-compromising diseases had highest 68.4% mortality (Table 2).

Odds ratio (ORs) were estimated for all variables by univariate logistic regression. All variables except coronary artery disease and HTN had unadjusted odds ratio higher than 1 with p value <0.05. Older age categories, male gender and patients having: diabetes mellitus, chronic kidney disease, malignancy and other immuno-compromising disease and delay in hospitalization, were statistically significant factors associated with mortality

(Table 3). All the significant study variables were further processed using a multivariable logistic regression. After this analysis, older age categories 45 to 60 years AOR 1.978 (95% CI=1.243-3.149) and age >60 years AOR 5.392 (CI=3.435-8.463) were found to be significant predictors of mortality. Among highly prevalent variables, delayed hospital admission AOR 8.204 (95% CI 5.522-12.188) and diabetes mellitus AOR 1.888 (95% CI=1.199-2.972) were found to be significant determinant of mortality. Among the less-frequent variables: malignancy and other immunocompromising diseases AOR 9.108 (95% CI=2.934-28.270) and CKD AOR 7.524 (95% CI=2.289-27.735) were the significant determinants of mortality (Table 4).

Table 1: Epidemiological and clinical profile of the hospitalized patients of COVID-19.

Variables	No. of patients (%)
Gender	
Male	438 (55.4)
Female	352 (44.6)
Age (years)	
>60	278 (35.2)
45-60	217 (27.5)
18-44	295 (37.3)
Diabetes	
Yes	139 (17.6)
No	651 (82.4)
Hypertension	
Yes	55 (7)
No	735 (93)
Coronary artery disease	
Yes	12 (1.4)
No	778 (98.5)
Chronic kidney disease	
Yes	15 (1.9)
No	775 (98.1)
Delayed admission	
Yes	337 (42.7)
No	453 (57.3)
Malignancy or other immune-compromising diseases	
Yes	19 (2.5)
No	771 (97.5)

Table 2: Mortality in different variables among the hospitalised patients of COVID-19.

Variables	No of deaths (mortality rate in the variable)	No. of recovered and discharged (recovery rate in the variable)
Gender		
Male	145 (33.1)	293 (66.9)
Female	90 (25.6)	262 (74.4)
Age (years)		
>60	122 (43.9)	156 (56.1)
45-60	64 (29.5)	153 (70.5)
18-44	49 (16.6)	246 (83.4)
Diabetes		
Yes	55 (39.6)	84 (60.4)
No	180 (27.6)	471 (72.4)
Hypertension		
Yes	14 (25.5)	41 (74.5)
No	221 (30)	514 (70)
Coronary artery disease		
Yes	6 (50)	6 (50)
No	229 (29.4)	550 (70.3)

Continued.

Variables	No of deaths (mortality rate in the variable)	No. of recovered and discharged (recovery rate in the variable)
Chronic kidney disease		
Yes	9 (60)	6 (40)
No	226 (29.2)	549 (70.8)
Delayed admission		
Yes	165 (49)	172 (51)
No	70 (15.5)	383 (84.5)
Maliganancy or other immune-compromising diseases		
Yes	13 (68.4)	6 (31.6)
No	222 (28.18)	549 (71.2)
Total	235 (29.7)	555 (70.3)

Table 3: Univariate analysis of the factors associated with mortality among hospitalised COVID-19 patients.

Factors	No. of deaths	Recovered/ discharged	Chi square	P value	OR (95% CI)
Age (years)					
>60	122	156	50.957	0.000	3.926 (2.665-5.784)
45-60	64	153		0.001	
18-44	49	246			2.100 (1.375-3.207)
Gender					
Male	145	293	5.305	0.021	1.441 (1.055-1.967)
Female	90	262			
Hypertension					
Yes	14	41	0.521	0.470	0.794 (0.424-1.486)
No	221	514			
Diabetes mellitus					
Yes	55	84	7.686	0.005	1.713 (1.171-2.508)
No	180	471			
Chronic kidney disease					
Yes	9	6	NA	0.018*	3.644 (1.282-10.356)
No	226	549			
Coronary artery disease					
Yes	6	6	NA	0.198*	2.397 (0.765-7.511)
No	229	549			
Malignancy and other immune-compromising diseases					
Yes	13	6	13.934	0.000	5.358 (2.011-14.274)
No	222	549			
Delay in hospitalization					
Yes	165	172	103.828	0.000	5.249 (3.764-7.319)
No	70	383			

*Fisher's exact test

Table 4: Predictors of mortality among hospitalized COVID-19 patients after multivariate logistic regression analysis.

Variable	P value	Adjusted odds ratio AOR (95% CI)
Gender		
Male	0.148	1.308 (0.909-0.1881)
Female[r]		
Age (years)		
>60	0.000	5.392 (3.435-8.463)
45-60	0.004	1.978 (1.243-3.149)
Diabetes		
18-44[r]		
Yes	0.006	1.888 (1.199-2.972)

Continued.

Variable	P value	Adjusted odds ratio AOR (95% CI)
Chronic kidney disease		
No[r]		
Yes	0.001	7.524 (2.289-27.735)
Delayed hospital admission		
No[r]		
Yes	0.000	8.204 (5.522-12.188)
Cancer and other immunocompromising diseases		
No[r]		
Yes	0.000	9.108 (2.934-28.270)

r=reference category

DISCUSSION

The mean age of our study population was 52.2 years (SD-17.3 years). Gandhi et al has found mean age to range from 39.7 to 54 years in most Indian studies.[7] Median age was observed to be 56 years in a study in China and 63 years in Italy.[8,9] This difference may be attributed to the fact that vaccination had started for people above 60 years before second wave of COVID. The present study confirmed the association of age with mortality as indicated in previous studies in different countries.[10] Older age and comorbidities such as hypertension and diabetes were highly prevalent in this study similar to the pattern reported in China.[11] Older age susceptibility has been linked to age-dependent defects on T-cell and B-cell function and increased production of type 2 cytokines that lead to deficiency in control of viral replication and prolonged proinflammatory responses.[12]

About 55.4% affected were males in our study which is comparable to a study from other countries.[13] The difference of outcome between males and females was not statistically significant, after adjusting for other variables, similar to the results observed in other Indian studies also.

Mortality rate among study participants in this study was 29.7% which is slightly higher than many other studies from India. The reason could be that most of those studies were done during which even mild cases were also being admitted to hospital. but during second wave only moderately and seriously ill patients were being admitted to dedicated covid hospitals, mild cases were either in home isolation or at COVID isolation centers. Mortality observed in our study is comparable to in hospital mortality throughout the world.[12,14] Comparable mortality rate 28.4% was observed in a study in Bihar, India in the similar study setting. Higher mortality 71.2% was observed in in a study in Pakistan.[15]

Delay in the hospital admission turned out to be the most prevalent and one of the significant predictors of mortality. Many patients were profoundly hypoxic and requiring respiratory support soon after admission. Many collapsed within 2-6 hours of admission indicating delayed hospitalization. This can be attributed to the 'silent hypoxia' observed in COVID-19 infection. Secondly, since mostly patients with COVID-19 infection have mild disease and recover without hospital admission, this might have misled others who had moderate illness to wait for self-recovery at home, leading to progression to severe disease. This study confirms the results observed in earlier studies in Bihar and other countries like England and Pakistan.[6,14,16]

The median time gap from onset of symptom to hospital admission was 7 days in this study. In different studies it has been found to range from 5 days to 14 days.[17] When patients get infected with COVID-19 virus, some of them develop mild disease and the symptoms start resolving by 4th-5th day and in others the disease worsens due to cytokine storms known to occur in COVID-19 patients.[18] If the patients: in whom disease progresses toward moderate or severe illness, seek treatment in hospitals at right time, then the mortality can be minimized or prevented.

Diabetes mellitus was the second most prevalent and significant predictors of mortality in this study. DM creates a hyperinflammatory state and impairs innate and cell-mediated immunity, which may predispose COVID-19 patients to the cytokine storm.

Furthermore, increased release of cytokines in patients of COVID-19 with diabetes, in blunted antiviral interferon responses and the delayed activation of T-helper1/Th17, may contribute to worse outcomes.[19,20] DM was found to be significant predictors of mortality in studies in other countries like in Island and Italy also.[16,21]

Among the less frequent comorbidities chronic kidney diseases and malignancy and other immuno-compromising diseases were the significant predictors of mortality. Similar results were observed in a study in India and in a study in China also.[22,23]

The association of CKD might be due to the fact that ACE2, the cell entry receptor of SAR-CoV-2 is expressed almost 100 times higher in the kidneys compared to lungs.[24]

CONCLUSION

DM and delayed hospitalization were most prevalent risk factors among hospitalised patients. Overall, five predictors of mortality were identified: higher age, hospitalization after 7 days of onset of symptoms, pre-existing concurrent DM, CKD and malignancy and other immunocompromising diseases. Patients who recovered were having lower median time gap of 5 days (IQR 3-8 days) between onset of symptoms and hospitalization compared to 9 days (IQR 7-11 days) among the patients who died. There is lack of right knowledge in society about timing for hospitalization or clinical consultation during COVID-19 disease.

To reduce the mortality in COVID-19 patients, targeted interventions focused on specific factor will lead to better results. Delay in hospitalization was a highly prevalent predictor of mortality in the study participants, to which not much importance has been given till now. Simple interventions like special counselling services for all COVID positive patients at the testing centres can reduce delayed hospitalization. Dedicated OPD services for patients having mild COVID-19 disease can reduce the progression in to severity, especially among patient with comorbidities and hence can reduce the mortality.

Strengths

We included all the patients admitted to the hospital, and analysed data using two regression models. Our findings are internally consistent and statistically significant.

Limitations

Date of onset of symptom was self-reported and the data is observational: the results might have been influenced by unmeasured confounders.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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