Original Article

Clinical Characteristics and Outcomes in Patients Admitted in ICU with Severe COVID-19 in a Tertiary Care Hospital in North India: A Retrospective Observational Study

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Abstract

Background: Many studies have reported poor clinical outcomes regarding the ICU course of patients with severe COVID 19. Our study aimed at prospectively observing the predominant clinical pattern and outcomes in patients with severe COVID 19 admitted in the ICU.

Materials and Methods: This study was a retrospective, observational study of 100 patients admitted to the ICU with confirmed COVID 19. Data from all patients with confirmed COVID 19 admitted in ICU between 15 March 2021 to 25 April 2021 was included for this study. Patients were studied for their demographics, baseline comorbidities, laboratory investigations, and details of treatment. Major outcomes analyzed were clinical presentation, mechanical ventilation (MV) related mortality, and overall mortality of ICU patients. Student's independent t-test for comparing continuous variables and Chi-square test for categorical variables.

Results: Out of 220 patients with COVID-19, 100 were admitted to the ICU. The most common comorbidities were hypertension (38) and diabetes (25). Twenty-eight patients required mechanical ventilation (MV), out of which only 16 survived. MV LOS was longer for survivors than non-survivors. The overall mortality rate in ICU patients was 25%, and MV-related mortality was 42.85%.

Conclusion: The severity of presenting symptoms and presentation time play a major role in the outcome. Our study reports higher mortality in patients who required mechanical ventilation. This could be because of the increased severity of disease in these patients.

Keywords: COVID 19, ICU outcomes, North India, Retrospective

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Introduction

Finding its origin in Wuhan, China, the Coronavirus disease 2019 (COVID-19) has affected more than 200 million people worldwide since December 2019. In India, the first confirmed case of COVID-19 was diagnosed on 30 January 2020. As of this writing, the raging pandemic has infected around 30 million people and claimed more than 400 000 lives in the country. Epidemiological studies show that most infected individuals remain asymptomatic or develop a mild flu-like illness with fever, chills, cough, and sore throat. Around 6 to 10% of patients develop severe disease and require ICU admission due to acute respiratory failure. Most of these patients develop acute respiratory distress syndrome (ARDS) and eventually require mechanical ventilation.

The majority of the ICU reports from the United States show COVID 19 associated ARDS (CARDS) with increased duration of mechanical ventilation and higher mortality (1). Case reports from Italy and China have pointed out extrapulmonary manifestations as a strong predictor of poor outcomes in extremely ill patients with CARDS (2, 3). In India, similar findings of poor prognosis and higher mortality were noted in patients who developed CARDS and received mechanical ventilation. The situation has been much worse in the densely populated megacities like Mumbai, New Delhi, Kolkata, and especially the slums where overcrowding, poor hygiene, and failure to observe appropriate covid behavior are major contributing factors.

As reported from different countries, mortality rates in patients suffering from COVID 19 are extremely variable. In the USA, reports from Seattle, California, and Washington have reported mortality rates of 50-65% (4-6). In patients on MV, mortality is as high as 97% (7). Similar high fatality and overburdening of ICUs were reported from France, Spain, and Italy. In India, the literature suggests lower ICU mortality rates than in the west. Whereas tertiary care centers in New Delhi reported a mortality rate of 8-18% (8); mortality of 16.7% (9) have been reported from centers in Maharashtra; the Indian state accounts for nearly one-third of the country's total case count.

Thus, it is clear that this disease behaves differently in different populations, so studying its behavior in the local population assumes significance as it can help in further understanding the nature of this pathogen. Hence, we decided to document the clinical demographic profile and outcomes in patients admitted in ICU with severe COVID 19 illness in one of the largest tertiary care facilities in Jammu and Kashmir, India.

This study documents the behavior of COVID 19 during the second wave and delineates some of the key factors that have an important effect on survival in COVID 19 patients. Our study talks about the experience of the second wave in a tertiary care institute with limited resources and thus assumes significance in the scenario of a developing nation like India, where new cases are being detected every day. This study could help many institutes deal with infrastructural and logistical problems.

Methods

After obtaining approval from the institutional ethics committee (IEC no- 146 dated 24 -7-2021), this single centered, retrospective, observational study was conducted in the anesthesia and intensive care department in one of the largest tertiary care hospitals in north India. All patients admitted to ICU between 15 March 2021 to 25 April 2021 with confirmed COVID 19 (confirmed by RTPCR done on naso/oropharyngeal swab) were included in this study.

Our institute served as a primary admission and referral center from nodal hospitals as per government policy. Patients of all grades of severity were referred to our hospital. The referred patients, as well as those presenting for the first time, were received in a screening area, evaluated as per guidelines (10), and triaged to the isolation ward, high dependency unit (HDU), or intensive care unit (ICU) as per clinical severity. Mild cases were kept in the isolation ward, whereas, moderate cases were shifted to HDU. Severe cases were defined as those with respiratory rate > 30/min, blood oxygen saturation< 93% on room air, Pao2/FIO2 < 300, and those with ARDS, confusion, disorientation, sepsis septic shock, multiorgan failure – defined as critical cases.

The patients fulfilling these criteria were admitted to the ICU, where treatment was given as per international (11) and institutional protocols. Oxygen therapy with the clinically appropriate devices and prone positioning ineligible patients were done. We adhered to the ARDS Network strategy (12) for patients requiring mechanical ventilation of low tidal volume, low PEEP, and high FIO2. The aim was to keep plateau pressures less than 30cm H2O and driving pressure below 15cm H2O. Patients were discharged only after two consecutive negative reports of RTPCR and resolution of clinical symptoms and chest x-ray changes.

Data collection- The following data were retrieved from the hospital records – demographic parameters- (age, sex, body weight) of all patients, medical history including underlying comorbidities, clinical symptoms, and signs, laboratory investigations (complete blood count, liver/ kidney function tests, chest X-ray, ECG, etc.), mode of respiratory support (oxygen by facemask, a high-flow nasal cannula (HFNC), non-invasive or invasive ventilation); MV LOS, ICU LOS among survivors and non-survivors and outcome (in terms of still admitted/discharge/death). Patient outcomes were followed up to 28 April 2021.

Statistical analysis- The compiled data were entered in a spreadsheet (Micro Excel) and then exported to the data editor of SPSS Version 20.0 (SPAA Inc., Chicago, Illinois, USA). Continuous variables were expressed as median (interquartile range IQR), and categorical variables were summarized as frequencies and percentages. The student's independent *t*-test was employed for comparing continuous variables. The Chi-square test was applied for comparing categorical variables.

Results

From 15 March to 15 April 2021, 100 patients were admitted to the ICU. Out of which, 65 were males, and 35 were females. The median age of patients included in this study was 45 years (IQR= 25-61). Most deceased patients belonged to the younger age group with a median age of 48years (IQR= 40-55). (Table 1)

Fever (85%), cough (50%), and dyspnea (10%) were the major presenting symptoms. Initial presenting symptoms of dyspnea (respiratory rate >30), SpO2 <90% on room air, and multiorgan involvement were more common in non-survivors. The median duration from first symptoms to dyspnea and hospital admission was 3 days (IQR= 0-5) and 9 days (5-14), respectively. A significant observation was the longest time to hospital admission from symptom onset in the non-survivor group (Table 1).

The most frequent comorbidities documented were hypertension (38) and diabetes (25). The number of patients with coronary artery disease (CAD) was 12(12%), chronic obstructive pulmonary disease (COPD)-14(14%), chronic kidney disease (CKD) - 11 (11%), and any other significant comorbidity (like chronic liver disease, associated malignancy) were 10(10%). The occurrence of comorbidities was higher in non-survivors than survivors. (Table1)

Chest X-ray was present for all 100 patients at ICU admission. Sixty-five patients (65%) showed bilateral involvement, 30 patients (30%) had unilateral involvement, whereas only 5 patients (5%) had a normal X-ray at the time of admission. Bilateral involvement was more common among the non-survivors. The most common presentation on CT was patchy bilateral shadowing (65%). Laboratory findings were commonly seen in patients with severe disease admitted in ICU were low counts of lymphocytes, T cells, higher counts of neutrophils, D dimer, C reactive protein, procalcitonin, blood urea nitrogen, and creatinine. However, the values of these parameters were significantly higher in non-survivors (Table1).

Table 1: Demographic characteristics, comorbidities, and laboratory parameters in survivors and nonsurvivors.

Parameters	**All patients (n=100)**	**Survivors (n=75)**	**Non survivors (n=25)**	**P value**
Age (in years)	45(25-61)	58 (55-61)	44(28-50)	<0.001
Sex (M/F)	65/35	45/30	15/10	>0.99
Time period from first symptom to hospitalisation(days)	9(5-14)	6 (5-8)	11(9-14)	<0.001
Comorbidities				
Hypertension(yes/no)	38/62	29/46	9/15	0.563
Diabetes(yes/no)	25/75	5/65	10/15	<0.001
CAD (yes/no)	12/88	6/69	7/18	0.634
COPD (yes/no)	14/86	4/71	10/15	<0.001
CKD (yes/no)	11/89	3/72	8/17	<0.001
Other co morbidities (yes/no)	10/90	3/72	7/18	<0.001
Laboratory findings				
Haemoglobin(g%)	9.8 (7-11)	9.8(8-11)	9.8(7-11)	0.462
Total leukocyte count (cells/µl)	1450(1350-13000)	1400(1350-9000)	2100(1900-13000)	<0.001
Absolute neutrophil count (cells/µl)	7052(4020-12500)	6500(4020-8600)	10200(6600-12500)	<0.001
Absolute lymphocyte count(cells/µl)	1388(1020-2100)	1280(1020-1570)	1804(1450-2100)	<0.001
D dimer (ng/ml)	225(75-396)	172(75-212)	258(196-396)	<0.001
Serum creatinine (mg/dl)	1(0.8-1.2)	1(0.8-1)	1.1(0.8-1.2)	0.282
Arterial lactate(mmol/l)	3.1(1.3-6.2)	2.2(1.3-3.4)	4.6(3.2-6.2)	<0.001
Radiologic findings				
Normal	5(5%)	5(5%)	0	<0.001
Lobar consolidation with bilateral infiltrates	65(65%)	20(20%)	45(45%)	<0.001
Patchy unilateral infiltrates	30(30%)	16(16%)	14(14%)	0.562
Clinical presentation				
Fever	85(85%)	60(80%)	20(80%)	0.876
Cough	50(50%)	34(45%)	12(48%)	0.565
Dyspnea	10(10%)	3(4%)	7(28%)	<0.001
SpO2(%)	88(79-95)	92(90-95)	86(79-90)	<0.001
Ventilation parameters				
PaO2/FIO2	185(132-239)	204(180-240)	169(135-195)	<0.001
PEEP (cm H2O)	9(7-12)	8(7-10)	10(9-12)	<0.001
MV LOS (days)	12(3-22)	18(8-22)	6(3-11)	<0.001
ICU LOS (days)	18(2-25)	21(5-25)	6(2-11)	<0.001

Data expressed as percentage or median (interquartile range), as applicable. Student independent t-test and chi-square test were used for statistical analysis. CAD- coronary artery disease, CKD-chronic kidney disease, COPD-chronic obstructive pulmonary disease, MV LOS- mechanical ventilation length of stay, ICU LOS-intensive care unit length of stay.

Table 2: ICU outcomes in patients with COVID-19.

Outcomes	N (%)
Still admitted	45(45%)
Discharged	30(30%)
Deaths	25(25%)
Deaths in patients on ventilator (MV related deaths)	12 (42.85%)
Overall ICU mortality	25(25%)

Out of 100 patients admitted in ICU, 28 (28%) received mechanical ventilation, 18(18%) received non-invasive ventilation, 8 (8%) received oxygen therapy with high flow nasal cannula (HFNC), while the rest received oxygen via face mask.

Compared to non-survivors, survivors had a longer time on the ventilator [18 days (IQR =8-22) versus 6 days (IQR=3-11)] and longer ICU LOS [21 days (IQR=5-25) versus 6.0 (IQR= 2-11)]. The average PaO2/FIO2 ratio was lower in non-survivors [169 (IQR=135- 195)] versus survivors [204(IQR=180-240)]. Lower Positive end-expiratory pressure (PEEP) averages were seen among the survivors – 8 cm H2O (IQR= 7-10) than non-survivors- 10cm H2O (IQR= 9-12) (Table 1).

At the end of the follow-up period, 45 patients were still admitted, while 30 were discharged. A total of 25 patients died, out of which 12 were on ventilators. Hence, MV-related mortality, as reported by our study, was 42.85%, while the overall ICU mortality was 25% (Table 2).

Data expressed as percentage or median (Interquartile range), as applicable. Student independent t-test and chi-square test were used for statistical analysis. CAD- coronary artery disease, CKD-chronic kidney disease, COPD-chronic obstructive pulmonary disease, MV LOS-mechanical ventilation length of stay, ICU LOS-intensive care unit length of stay.

Discussion

We reported the clinical characteristics, hospital course, and outcomes in 100 patients admitted in ICU of a COVID 19 dedicated hospital in North India. Compared to previous studies done by various workers (13), the average age of presentation in our patients was lower. There was a larger male preponderance in our study; this can be explained by the fact that these patients were part of large public congregations which occurred during the festive season and were predominantly attended by males.

The mean time is taken to present to the hospital after the first symptoms appeared longer in nonsurvivors than survivors. The delay in arriving at the hospital is multifactorial. It could be due to ignorance, careless attitude to one's wellbeing and safety of the family, fear of social stigma, overburdening of hospitals and ICUs leading to a dearth of beds leading to late admission or death before admission. Also, co-morbidities like diabetes mellitus (seen in as high as 25% of patients in our study) impair the perception of dyspnea leading to delay in seeking medical attention (14). Early hospital admission and timely treatment, therefore, play a very important role in improving the prognosis of this disease.

Fever and cough were the predominant presenting complaints in survivors whereas dyspnea at first presentation was more frequently observed among nonsurvivors. Oxyhemoglobin saturation (SpO2) and respiratory rate at the time of presentation also served as important predictors of mortality in our study, with survival rate being lower in patients with respiratory rate >30 (tachypnea) and SpO2<90% on room air. Mohan A et al (13) and Kayina CA et al (8), who examined the clinical course of COVID19 in their respective centers, also emphasized the potential role of tachypnea and low oxyhemoglobin saturation in affecting patient outcomes. This assumes significance in COVID 19 because the unique pathophysiology of this disease gives rise to "happy hypoxemia". Most of the patients do not complain of dyspnea even in the presence of alarming levels of hypoxemia.

Dyspnea is defined as a sensation of difficult or labored breathing, which occurs when the demand for ventilation is out of proportion to the patient's ability to respond. Therefore, it is different from tachypnea (rapid breathing) and hyperpnea (increased tidal ventilation). COVID 19 patients usually present with hypoxia (low PO2) and low CO2. Respiratory chemoreceptors are highly sensitive to increased PaCO2 levels, whereas hypoxemia plays a minor role in the sensation of breathlessness. Experimental models have shown that dyspnea only occurs when PaO2 drops below 40 mmHg, whereas at PaO2 levels between 65 and 40 mmHg, there is a rise in minute ventilation, increase in the respiratory rate, without dyspnea. Therefore, as highlighted in our study, tachypnea, and hyperpnea, not dyspnea, are the clinical signs of impending hypoxemic respiratory failure. (15, 16) Though not routinely present, dyspnea in COVID-19 patients should alert the clinician, as it indicates deterioration and failing lung compliance (17).

A keen study of laboratory investigations highlights a higher incidence of lymphopenia and increased count of neutrophils among the non-survivor group. Our results are similar to Guan WJ et al. (14) and Huang C et al. (18), who reported lymphopenia as a predictor of severe disease. Similarly, the high neutrophil count has been reported as a marker of poor prognosis by Terpos E et al. (19). On the other hand, Mohan A et al. (13) reported that lymphopenia was not associated with poor prognosis in their study; Oliveira E et al. (20), while describing their experience with COVID 19 in Central Florida, did not observe any significant difference in neutrophil count between survivors and non-survivors.

However, more than the solitary values of these laboratory parameters, the trend of their serial values is more important in monitoring clinical course in these patients. However, because of the high patient load and limited resources in our institute, repeat tests were not done in all patients, and the intensivists relied on the clinical features for monitoring response to treatment in these patients. Thus, as already discussed above, symptoms like fever (indicative of cytokine storm), dyspnea(indicative of respiratory decompensation), important signs like tachypnea, and decreased oxyhemoglobin saturation assume increased significance in the scenario of a developing country as they become the cornerstone of patient management and outcome.

In our study, chest X-ray changes were seen in almost all patients with severe disease, with only 5 patients reporting no x-ray changes. The most common presentation was lobar consolidation with bilateral infiltrates. The pathophysiology of COVID 19 pneumonia is characterized by type 2 alveolar hyperplasia, endothelial dysfunction, and hyperplasia of interstitial capillaries with macro and microthrombi formation. Gattitoni et al. (21) published a very interesting paper titled: COVID 19 pneumonia- ARDS or not. They proposed the existence of two pathophysiological types of COVID 19 ARDS- type L (light phenotype) and type H (heavy phenotype). Type L is characterized by normal lung compliance and has a unique behavior akin to other respiratory diseases. Type H has high lung elastance, is associated with severe disease, and resembles classical ARDS. These histopathological features are mirrored in the HRCT findings.

While 18 patients required non-invasive ventilation, 8 received oxygen via HFNC. Twenty-eight patients who landed on mechanical ventilation were in severe COVID 19 associated ARDS with mean PaO2/FIO2 <185 (132-239); values as low as 169(135-195) were seen in non-survivors. We followed the ARDS ventilation protocol with high FIO2, low PEEP, and low tidal volumes to keep plateau pressures <30cmH2O. Patients requiring higher PEEP showed poor survival. The mortality rate was high in patients on mechanical ventilation in our study. Our results were similar to Grasselli G et al. (22) and Richardson S et al. (1); however, workers like Mohan A et al. (13) recorded lower mortality rates. The high mortality associated with mechanical ventilation in our study can be explained because these patients were admitted during the second wave caused by the delta variant. This highly infective variant resulted in rapid decompensation (transition from L to H phenotype) and higher mortality in the younger age group than the first wave, where those with advanced age and significant comorbidities showed grave prognosis. Another contributing factor to the high mortality could be late hospital admission, as most of these patients consulted only after the disease had progressed to its advanced stage.

This study has a few limitations, for example, there was no follow-up after discharge, and if the patient got re-admitted to another facility, the authors would not know, and certain other significant unmeasured factors could affect the outcomes and survival.

Conclusion

The severity of presenting symptoms, especially tachypnea and oxyhemoglobin saturation, and time of presentation to the hospital play a very important role in predicting the outcome in COVID-19 patients. Dyspnea, if present, should take as a red flag sign as it indicates respiratory decompensation. CARDS is associated with a higher incidence of mechanical ventilation and subsequent mortality.

Acknowledgment

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Conflicts of Interest

The authors declare that they have no conflict of interest.

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