Original Article

Epidemiology and clinical characteristics of COVID- 19 patients requiring critical care in a Tertiary care teaching hospital

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Abstract

Background and Aims: We describe the epidemiological and clinical characteristics, and 28 day outcome of critically ill COVID-19 patients admitted to a tertiary care centre in India.

Material and Methods: We included 60 adult critically ill COVID-19 patients in this prospective observational study, admitted to the intensive care unit (ICU) after obtaining ethics committee approval and informed consent. Demographics, clinical data, and treatment outcome at 28 days were assessed.

Results: Demographic characteristics of the COVID-19 patients reveal that compared to the survivors, the non-survivors were significantly older [57.5 vs. 47.5 years], had more comorbid disease [Charlson's comorbidity index 4 vs. 2], higher Apache II scores [19 vs. 8.5], and had significantly higher percentage of smokers. Diabetes mellitus and hypertension were the most common comorbidities. Dyspnea, fever, and cough were the most common presenting symptoms. Total leucocyte count as well as blood lactate level were significantly higher in non-survivors. Around 47% patients had severe ARDS, and 60% patients required invasive mechanical ventilation. 28 day ICU mortality was 50%, with a mortality of 75% in patients receiving invasive mechanical ventilation. Mortality was higher in males than females (57% vs. 33%). Acute kidney injury and septic shock were the most common non-pulmonary complications during ICU stay. Incidence of liver dysfunction, septic shock, and vasopressor use was significantly higher in the non-survivors.

Conclusion: This study demonstrates a high 28 day mortality in severe COVID-19 patients. Further well designed prospective studies with larger sample size are needed to identify the risk factors associated with poor outcome in such patients.

Keywords: ARDS, COVID-19, critically ill, SARS-Cov-2

Introduction

The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV2) originated in Wuhan, China, in December 2019,[1] causing coronavirus disease 19 (COVID-19), with clinical manifestations resembling viral pneuzmonia. Phylogenetically, it is closely related to the SARS-like coronaviruses originating from bats.[2] Although early reports described the disease as SARS like atypical pneumonia, with 26–33% of patients requiring intensive care admission and a mortality of 4–15%,[1,3,4] a later large case series of 72,314 patients from China has estimated the same to be 14% and 2.3%, respectively.[5] Subsequently, large data from USA, Italy, China, and Spain[6] have emerged, describing the

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epidemiology and clinical outcomes of COVID-19 patients. India is the 2nd worst affected nation, with more than 32 million cases and 43 thousand deaths.[7] This study aimed to assess the epidemiological and clinical characteristics of critically ill COVID-19 patients admitted to a tertiary care teaching hospital in India.

Primary objective of this study was to assess ICU mortality in COVID-19 patients (28 days) admitted to the intensive care unit of AIIMS, New Delhi.

The secondary objectives were
1. To know the incidence of ARDS, AKI, cardiac injury/dysfunction in COVID-19 patients
2. Incidence of prolonged ICU stay (more than 2 weeks)
3. Risk factors associated with poor outcome.

Material and Methods

After obtaining permission from the institute ethics committee and informed consent from their legally acceptable representatives, approximately n = 60 adult patients, of either sex, fulfilling WHO case definition of COVID-19 and admitted to an ICU at AIIMS, New Delhi, were included in the study. Patients or relatives who refused to provide consent or have unproven or suspected COVID- 19 infection were excluded from this study.

The following data were collected
1. Demographic parameters (age, sex, presence of comorbidities, drug history)
2. Clinical presentation
3. Baseline laboratory parameters
4. Clinical outcome and treatment [organ dysfunction, use of non-invasive (NIV) and invasive mechanical ventilation (IMV), mortality, length of intensive care unit (ICU) stay].

Standard intensive care management protocol of the institute was followed and standard management of respiratory failure and acute respiratory distress syndrome were followed in all patients. Protocolized weaning and extubation were also done. Fluid and vasopressor management were guided by hemodynamic variables and point of care ultrasound.

No formal sample size estimation was performed as no previous study was available in Indian population. All collected data were entered in a spreadsheet (Microsoft Excel). Statistical analysis was performed in STATA version 13 for Mac OS X (StataCorp. 2011. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP). Normality was tested by Shapiro–Wilk test. Normally distributed data were presented as mean and standard deviation (SD) and skewed data as median (interquartile range). For comparison of related samples, the paired and unpaired *t*-test were used for normally distributed data, and the Wilcoxon signed rank test and Mann–Whitney U test for skewed data.

Results

Data from $n = 60$ adult patients were analyzed. All patients had severe or critical COVID-19 disease. The demographic characteristics of the COVID-19 patients reveal [Table 1] the median age to be significantly higher in non-survivors [57.5 vs. 47.5 years]. The non-survivors had a significantly elevated APACHE II score and Charlson's comorbidity index at baseline. Diabetes mellitus and hypertension were the most common comorbidities present. Of note, smoking and alcoholism were significantly more common in non-survivors than survivors. Among the baseline laboratory parameters, total leucocyte count was significantly higher in non-survivors. Blood lactate level was significantly higher in non-survivors. Il-6 was obtained in eight patients, with a median value of 103 pg/ml [44–178].

Dyspnea, fever, and cough were the most common presentations. Clinical outcomes and treatment received, have been described in Table 2. At presentation, severe ARDS was found in 46.67% patients. High flow nasal cannula and/or noninvasive ventilation was used in 56.7% patients, and was comparable in both the groups. Thirty six (60%) patients required invasive mechanical ventilation during their ICU stay. NIV/HFNC failure was seen in 16.7% patients. Mortality in patients receiving invasive mechanical ventilation was 75%. On chest X-ray, majority of the patients had bilateral pneumonia, with only 3 patients having unilateral pneumonia. Involvement was primarily interstitial, with 12 (20%) developing consolidation during their ICU stay. Forty three (71.7%) patients underwent self-prone positioning during HFNC, NIV use or oxygen therapy. Of the patients receiving mechanical ventilation, 20 patients with severe ARDS underwent prone positioning, with a mean of 2.7 prone sessions. Mortality in severe ARDS was 71.4%, whereas it was 31.2% in both mild and moderate ARDS. Mortality among males was 57% as compared to 33% in females. Median length of ICU stay was 9 days, with prolonged ICU stay in 11 patients, and 3 patients still remaining in ICU at the end of study period. Acute kidney injury and septic shock were the most common non-pulmonary complications during ICU stay. Incidence of liver dysfunction, septic shock, and vasopressor use were significantly higher in the non-survivors. Four patients developed tachyarrhythmias (atrial fibrillation, ventricular trigeminy, ventricular tachycardia). Use of hydroxychloroquine, doxycycline or azithromycin, vitamin

Table 1: Baseline demographic characteristics and laboratory investigations in survivors and non- survivors

Parameter	All Patients (*n*=60)	Survivors (*n*=30)	Non- Survivors (*n*=30)	Significance
Age	50 [37.5-63]	47.5 [37-51]	57.5 [42-70]	*P*=0.034
Sex [M/F]	42/18	18/12	24/6	*P*=0.158
BMI	25.4 [22.55-28.65]	24.3 [22-29.5]	25.85 [24-28]	*P*=0.178
Apache II	13 [7.5-21.5]	8.5 [5-16]	19 [11-23]	*P*=0.0014
SOFA (*n*=60)	1 [1-2]	1 [1-1]	1 [1-2]	*P*=0.0345
Comorbid Illness/condition				
Charlson's comorbidity index	3 [2-5]	2 [1-4]	4 [3-5]	*P*=0.0039
Hypertension (yes/No)	21/39	12/18	9/21	*P*=0.589
Diabetes Mellitus (yes/No)	27/33	15/15	12/18	*P*=0.604
CKD (yes/No)	8/52	5/25	3/27	*P*=0.706
CLD (Yes/No)	8/52	2/28	6/24	*P*=0.254
Malignancy (yes/No)	8/52	4/26	4/26	*P*>0.99
Smoking (yes/No)	24/36	4/26	20/10	*P*<0.0001
Alcoholism (yes/no)	19/41	5/25	14/16	*P*=0.025
ACE/ARB use (yes/no)	4/56	3/27	1/29	*P*=0.612
Fever	37	17	20	*P*=0.596
Cough	24	16	8	*P*=0.064
Dyspnea	38	20	18	*P*=0.789
Sore throat	5	2	3	*P*>0.99
Laboratory Investigations				
Hemoglobin (*n*=60)	9.4 [7.95-12.1]	9.3 [8-12.5]	9.5 [7.9-11.3]	*P*=0.790
Total Leucocyte Count (*n*=60)	10450 [6350-14965]	9650 [5800-11250]	11550 [8250-18700]	*P*=0.0251
Platelet Count (*n*=59)	146 [89-218]	126 [95-203]	177 [72-228]	*P*=0.375
INR (*n*=47)	1.2 [1-1.4]	1.1 [1-1.35]	1.3 [1.3-1.73]	*P*=0.148
Serum Creatinine mg/dl (*n*=60)	1.2 [0.75-2.65]	0.95 [0.8-1.6]	1.38 [0.7-3]	*P*=0.402
Serum Urea mg/dl (*n*=59)	40 [28-80]	39.5 [28-52]	41.4 [31-94]	*P*=0.309
Serum Na+ meq/L (*n*=60)	141.4 [133.5-141.4]	139 [134-141]	138.5 [133-141.8]	*P*=0.917
Serum K+ meq/L (*n*=60)	4.2 [3.65-4.8]	4.15 [3.6-4.7]	4.4 [3.8-5.4]	*P*=0.227
Serum Alb g/dl (*n*=46)	3.1 [2.3-3.3]	3.1 [2.2-3.6]	3.1 [2.4-3.3]	*P*=0.884
Serum Bilirubin mg/dl (*n*=41)	0.9 [0.5-1.9]	0.8 [0.4-1.1]	1.5 [0.6-3.4]	*P*=0.0413
ALT IU/L (*n*=56)	47 (31-66.5)	47 [31.5-70]	49.5 [31-65.5]	*P*=0.550
AST IU/L (*n*=43)	48 [27-87]	48 [25-71]	49.5 [29-88.5]	*P*=0.677
Blood Glucose (mg/dl) (*n*=42)	164 [130-220]	173.5 [132-220]	149 [130-210]	
Lactate mmol/L	1.4 [1-2.4]	1.2 [0.9-1.5]	2 [1.4-4.2]	*P*=0.0058
Bilateral pneumonia (yes/no)	57/3	30/0	27/3	*P*=0.076

Table 2: Clinical outcome and treatment. Data expressed as proportion or median [IQR]; Mann Whitney U test or Fisher exact test applied as applicable

Parameter	ALL	Survivors (30)	Non-survivors (30)	Significance
ARDS severity at presentation [Mild/moderate/severe]	16/16/28	11/11/8	5/5/20	*P*=0.009
Length of ICU stay (*n*=57)	9 [4-13]	9 [5-14]	8.5 [3-13]	
AKI (*n*=60)	27	10	17	*P*=0.119
Cardiac dysfunction (*n*=60)	4	1	3	*P*=0.612
Liver dysfunction (*n*=60)	8	1	7	*P*=0.052
Septic shock (*n*=60)	22	1	21	*P*<0.0001
Vasopressor use (*n*=60)	29	4	25	*P*<0.0001
HCQ (*n*=60) use	51	27	24	*P*=0.47
Azithro/Doxy (*n*=60) use	56	30	26	*P*=0.112
Initial NIV use	21	11	10	*P*>0.99
HFNC use	13	7	6	*P*>0.99
RRT use	11	3	8	*P*=0.181

C, and zinc were similar in both the groups. All patients received the steroid methylprednisolone. Three patients received remdesvir, two patients lopinavir and ritonavir, and two patients got tocilizumab.

Discussion

In this epidemiological data from 60 patients, we observed that majority of patients were males, presenting with SARI symptoms. Majority required invasive mechanical ventilation, and 50% died within the 4 weeks of ICU admission. Mortality was higher in males compared to females. The median age of our cohort was similar to that of China [median 47 years],[8] but much younger than that of USA [median age 68 years][9] or Italy [median age 63 years].[10] Sex ratio was similar to the previously observed data. Admission APACHE II score was significantly higher in non-survivors than in survivors [19 vs. 8.5]. In a recent retrospective analysis by Zou *et al*., APACHE II score >17 effectively predicted mortality in COVID-19 patients.[11] Charlson's comorbidity index (CCI) was also significantly higher in the non-survivors [median 4 vs. 2], and was similar to CCI reported in hospitalized patients from USA.[8] This represents significant comorbidity in the non-survivors, with an estimated 10 years survival of 53%. A Danish study demonstrated that CCI more than 0 was associated with severe COVID-19 and death, with CCI of 3-4, and >4 having an odd's ratio of death being of 3 and 3.85, respectively.[12] Diabetes mellitus and hypertension were found to be the most common comorbidities, similar to a recent preliminary report from India.[13] However, ACE/ARB use was seen in only 6.6% patients. As in our study, smoking has been associated with severe disease, ICU admission, mechanical ventilation, and death,[14] by upregulating the ACE 2 receptor gene required for viral entry. Although the total leucocyte counts were significantly higher in the non-survivors, evidence for microbiologically proven bacterial infection was lacking. This finding was congruous with a retrospective review of non-survivors from a single center in Wuhan,[15] where the median TLC was 11.01×10^9 cells/L. The non-survivors also had an elevated blood lactate level,[15] similar to our study, thereby highlighting the importance of blood lactate estimation in critically ill COVID-19 patients. Mortality in our severe COVID ARDS cohort, as well as deaths in patients receiving invasive mechanical ventilation, were comparable to the mortality reported in patients who received invasive mechanical ventilation (IMV) in published data from China [79%],[16] and USA where it was 76.4% in the age group 18–65 years and 97.2% in older than 65 years.[9] However, data from Italy shows ICU mortality among patients who died, or got discharged to be 26%, with higher death rated among older patients. Spain and Denmark have also reported ICU mortality to be 29.2% and 41.2%, respectively. In a cohort of 24 ICU patients from western India, 5 week mortality was reported to be 16.7%.[17] However, no baseline disease severity was reported. The varying mortality rates may be reflective of the variations in comorbid disease burden, of baseline disease severity, differential thresholds for use of NIV, HFNC, or IMV, availability and use of ECMO, use of supportive pharmacological therapy, and factors related to race and ethnicity.

Limitations

Our study recruited a limited cohort of ICU patients. Lack of complete laboratory data is also a serious concern. Due to a small sample size, univariate and multivariate analysis could not be performed.

Conclusion

To conclude, this single tertiary care center prospective cohort of ICU patients from India demonstrates a high 28 day mortality rate in patients with severe COVID ARDS. Further well planned prospective studies with larger sample size are needed to identify the risk factors associated with poor outcome in such patients.

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Conflicts of interest

There are no conflicts of interest.

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