ORIGINAL ARTICLE

Clinical Characteristics and Outcomes of COVID-19 Patients Hospitalized in Intensive Care Unit

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Abstract

Background: Meta-analysis and clinical studies suggest coronavirus disease-2019 (COVID-19) patients in ICU have a high mortality rate of 30–45%, which has evolved as a function of criteria of admission and the management modalities.

Materials and methods: We conducted a retrospective evaluation for characteristics and outcomes in critical care set up across six months.

Results: 514 patients (74.3% males and 25.6% females) were evaluated. 9.72% ($n = 50$) patients expired, 78% ($n = 39$) were males. Mean age (years) was 57 (±14, range 64, 95% CI 55–58). 65.7% ($n = 338$) were of age more than 50 years, of which 71.5% ($n = 242$) were males. Males at 20% higher risk for death than women. (RR = 1.2, 95% CI 0.66–2.31, $p = 0.61$ NS). There was 18% less risk of mortality in female vs male with comorbidities (RR 0.82, 95% CI 0.67–1.12, $p = 0.32$ NS). Risk for mortality in diabetics was significantly increased by 116% vs nondiabetics. (RR 2.16, $p = 0.0055$, 95% CI 1.28–3.67). Highly significant risk of mortality in age group >50 years (3.13 times higher) vs age ≤50 years. (RR 3.18, 95% CI 1.71–8.64, $p = 0.0003$). 50.2% had moderate ARDS at admission. High flow nasal cannula was used in 47.2%. There is 5.79 times more likelihood to be on the ventilator with moderate to severe ARDS vs mild ARDS (RR = 5.79, 95% CI 3.10–11.05, $p < 0.0001$). Risk for death was six times higher for patients on ventilator vs not on ventilator (RR = 6.08, 95% CI 3.49–10.59, $p < 0.0001$). The mean number of days on ventilator for patients who underwent tracheostomy ($n = 49$) was 14 days as compared to 6.6 days in patients who were extubated ($n = 57$) ($p < 0.0001$). P/F ratio had negative correlation with number of days of hospitalisation (Pearson r -0.391, 95% CI -0.46– -0.31, $p < 0.0001$). 67% less chances of mortality in patients on steroids (RR = 0.33, 95% CI 0.19–60, $p = 0.0012$). Mean duration of ICU stay (days) was 8 (± 5, range 29, 95% CI 7.5–8.4).

Conclusions: We observed that a strict adherence to the basic principles of ARDS management resulted in a lower mortality in ICU setting.

Keywords: COVID-19, ICU, Outcomes.

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Introduction

The first case of coronavirus disease-2019 (COVID-19) attributed to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral infection was described in Wuhan in December 2019, China, and was declared as a pandemic by the World Health Organization on March 11, 2020. The initial reports suggest that 30% of patients require intensive care unit (ICU) admission, and the case fatality rate estimate was 2.3–7.2%. Hypoxemic respiratory failure is attributed as the most important reason for ICU admission.

Most of these patients require critical care support because of respiratory failure or the presence of multiorgan dysfunction syndrome. As there is no pharmacological therapy available, respiratory support in the form of supplemental oxygen, noninvasive ventilation (NIV), and invasive mechanical ventilation remains the mainstay of care in ICUs.

The factors associated with ICU admission include increased age, the presence of comorbidities, and cytokine storm. Initially, the case series and retrospective trials assessed proposed treatments. This has now evolved to the evaluation of the protocols through randomized controlled trials. Meta-analysis and clinical studies suggest COVID-19 patients in ICU have a high mortality rate of 30–45%, which has evolved as a function of criteria for admission and the management of modalities.[1–4]

As the pandemic spreads across the world, the manifestations and presentation of the disease also kept changing with time. Mumbai emerged as the epicenter of coronavirus infection in the country with an exponential increase in cases, as days progressed.

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Being a tertiary care center with dedicated COVID-19 ICU and wards, we had different groups of patients with varied manifestations admitted to the critical care unit, which led to different challenges during the treatment.

We evaluated COVID-19 patients who were admitted to our critical care unit for the various characteristics, including demographics, treatment modalities, and the outcomes of the critically ill patients. This is a single-center, retrospective observational study of 266 patients from the tertiary care ICU describing the demographic details, oxygenation method that includes high flow nasal oxygenation, invasive ventilation and NIV, awake prone ventilation, and the management of cases with outcomes.

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Materials and Methods

We conducted a retrospective evaluation of the patients ($n = 514$) who were admitted to the critical care setup at a tertiary care setting in Mumbai during the period from March 23, 2020, to September 10, 2020. This is a retrospective observational study of the patients in the critical care unit of a tertiary care ICU at Fortis Hospital Mulund in Mumbai. The hospital has a separate COVID-19 care block with wards and ICUs. The study was approved by the Institutional Ethics Committee. The patients were confirmed to be COVID-19 by reverse transcription-polymerase chain reaction from the nasopharyngeal and throat swab.

The objective of the study was to evaluate the various parameters that include the following:

- Demographics
- Correlation with the preexisting medical conditions
- P/F ratio at admission to ICU
- Utilization of various modalities of oxygenation, including ventilators
- The duration of stay in the ICU
- Effectiveness of various treatment modalities, including interleukin receptor blockers, corticosteroids, and antivirals
- Secondary infections
- Mortality outcomes

The aim of the study was to analyze the incidence of the COVID-19 cases in ICU among different age-groups and its relationship with preexisting medical conditions, P/F ratio at admission to ICU, methods of oxygenation, duration of stay in ICU, the effect of interleukin receptor blocker like tocilizumab (TCZ), secondary infections among patients, and the overall outcome of the patients. GraphPad was used for the statistical analysis.

Results

A total of 514 patients (74.3%, 382 males; and 25.6%, 132 females) were evaluated. Fifty patients expired (9.72%), and the rest recovered and discharged. The mean age (years) of the patients was 57 (±14; minimum, 23; maximum, 87; range, 64; 95% CI, 55–58), and 65.7% ($n = 338$) of patients were of age more than 50 years, of which 71.5% ($n = 242$) were males.

There were the highest number of patients in the age-group of 40–60 years (46.8%), of which the majority were males ($n = 189$, 78.4%). There were 41.6% of patients who were more than 60 years of age. There were a relatively lower number of younger patients admitted to ICU (11.4%). However, the proportion of patients who were young males was the highest ($n = 45$, 76.2%) (Table 1).

In the entire cohort ($n = 514$), there were 7.59% who died were men ($n = 39$) and 2.14% were women ($n = 11$). There was not any significant difference in the mortality across genders. However, males (10.21%) had numerically higher mortality as compared to females (8.33%). Men were at 20% of higher risk for death than women (RR = 1.2; 95% CI, 0.66–2.31; $p = 0.61$ NS) (Table 2).

Nearly, 82.05% of the males who died had comorbidities. There was no mortality in females who did not have any comorbidity. Females had mortality only in the presence of the comorbidities. There was 18% of less risk of mortality in females as compared to males with comorbidities (RR, 0.82; 95% CI, 0.67–1.12; $p = 0.32$ NS). Seven males (17.9%) who died did not have any comorbidities (Table 3).

There was a total of 200 diabetics (38.9%). The mortality was higher in diabetics (14.5%) as compared to nondiabetics (6.69%). The risk for mortality in diabetics was significantly increased by 116% as compared to the nondiabetics (RR, 2.16; $p = 0.0055$; 95% CI, 1.28–3.67). Among the patients who died ($n = 50$, 9.72%), 58% ($n = 29$) were diabetics (Table 4).

Nearly, 75.86% of the males who died had comorbidities ($n = 22$). There was 12% of lower risk of mortality in diabetic women as compared to the men who had diabetics (RR, 0.88; 95% CI, 0.56–1.67; $p = 0.74$ NS). Seven males (17.9%) who died did not have any comorbidities (Table 5).

There was a highly significant risk of mortality in the age-group >50 years (3.13 times higher) as compared to age ≤50 years (RR, 3.18; 95% CI, 1.71–8.64; $p = 0.0003$). And 63.3% ($n = 294$) of the patients who recovered were of age >50 years (Table 6).

Nearly, 87.18% of the men who died were of age >50 years ($n = 34$). There was 8% of lower risk of mortality in women >50 years

Table 1: ICU admissions across gender and age-groups

Age-groups	*Female*	*Male*	*Total*	*Percentage*
<40 (young)	14	45	59	11.4
40–60 (middle)	52	189	241	46.8
>60 (elderly)	66	148	214	41.6
Total	132	382	514	100

Of the total of 50 patients (9.72%) who expired, 78% ($n = 39$) were males

Table 2: Comparison of the mortality based on gender

	Mortality	*Discharged*	*Total*
Males	39	343	382
Females	11	121	132
Total	50	464	514

Table 3: Comparison of mortality based on the gender and comorbidities

Comorbidities	*Yes*	*No*	*Total*
Males	32	7	39
Females	11	0	11
Total	43	7	50

Table 4: Comparison of mortality based on the diabetes

	Mortality	*Discharged*	*Total*
Diabetics	29	171	200
Nondiabetics	21	293	314
Total	50	464	514

Table 5: Comparison of mortality based on the gender and diabetes

	Diabetics	*Nondiabetics*	*Total*
Males	22	17	39
Females	7	4	11
Total	29	21	50

A total of 44 patients (88%) who died were of age >50 years

Table 6: Comparison of mortality based on the age-groups

Age	*Mortality*	*Discharged*	*Total*
>50	44	294	338
≤50	6	170	176
Total	50	464	514

Table 7: Comparison of mortality based on the age-groups and gender

Age	*Male*	*Female*	*Total*
>50	34	10	44
≤50	5	1	6
Total	39	11	50

as compared to men >50 years (RR, 0.92; 95% CI, 0.70–1.79; p >0.99 NS). Only one female died at the age ≤50 years (Table 7).

There were existing comorbid conditions. There were a total of 200 diabetics (38.9%) followed by hypertension of 31.6%, cardiovascular disease (CVD) of 10.9%, chronic kidney disease (CKD) of 5.2%, and pulmonary disease of 3.7%. The other patients mainly included were pregnant patients and patients with a history of stroke and endocrine disorders.

PaO_2/FiO_2 (P/F) Ratio at ICU Admission

Since most of the patients had lung involvement and the majority presented to ICU with respiratory failure, the severity was assessed on basis of P/F ratio (PaO_2/FiO_2 ratio), at hospitalization. The patients were categorized as no acute respiratory distress syndrome (ARDS), mild ARDS, moderate ARDS, and severe ARDS with P/F ratios >300, 200–300, 100–199, and <100, respectively, based on the Berlin definition.[5]

The mean P/F ratio was 185 (±86, minimum, 38; maximum, 500; range, 462; 95% CI, 178–193). The mean P/F ratio in the males and females was 184 (±85, minimum, 184; maximum, 500; range, 462; 95% CI, 175–193) and 188 (±88, minimum, 50; maximum, 500; range, 450; 95% CI, 173–204; p = 0.613 NS). Most of the patients had moderate ARDS (50.2%), followed by mild ARDS (27.6%). There were 8.8% of the patients with P/F ratio greater than 300 but still required ICU admission. The difference between the P/F ratio at hospitalization in men as compared to women was comparable (p = 0.613 NS). Men had a relatively higher incidence of mild ARDS (78.1%) as compared to females across any other grade of ARDS. The percentage difference in the number of patients without ARDS across gender was the least, with 37.7% of women (Table 8).

Oxygenation Methods

High flow nasal cannula (HFNC) was used in 47.2% of patients followed by invasive ventilation and nasal prongs in 25.8 and 16.5%, respectively. On subgroup analysis, invasive ventilation was used in 93.18% of patients with severe ARDS. In cases with moderate ARDS, HFNC was used in 69.53% of patients and invasive ventilation in 17.18% of patients. In cases with mild ARDS, nasal prongs and HFNC were used in 47.22 and 44.44% of patients, respectively. Patients admitted to ICU with P/F ratio >400 were patients with road traffic accident–head injury, polytrauma, stroke, incidental COVID-19 in patients with diabetic ketoacidosis, and pregnant females (Table 9, Figs 1 and 2).

Table 8: P/F ratio of the patients on admission to ICU based on gender

P/F ratio (ARDS grading)	*Female*	*Male*	*Total*	*Percentage*
>300 (no ARDS)	17	28	45	8.75
200–300 (mild ARDS)	31	111	142	27.62
100–199 (moderate ARDS)	67	191	258	50.1
<100 (severe ARDS)	17	52	69	13.42
Total	132	382	514	100

Table 9: Different oxygenation methods across the cohort

Oxygenation method	*n (%)*
HFNC	243 (47.2)
Ventilator	133 (25.8)
NP	85 (16.5)
NIV	21 (4.08)
NRBM	14 (2.72)
RA	13 (2.52))
ECMO	1 (0.19)
FM	1 (0.19)
NIL	3 (0.58)
Grand total	514 (100)

ECMO, extracorporeal membrane oxygenator; HFNC, high flow nasal cannula; NIV, noninvasive ventilator; NP, nasal prongs; NRBM, non-rebreathing mask; RA, room air; FM, face mask

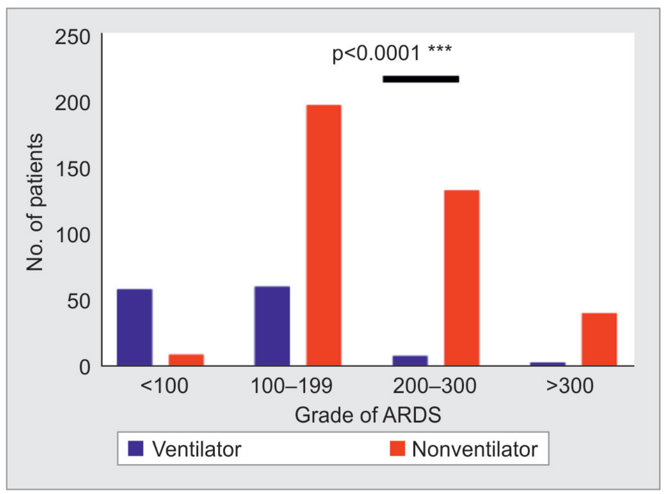

Fig. 1: Different oxygenation methods across the cohort

There was 5.79 times more likelihood to be on the ventilator for the patients with moderate to severe ARDS as compared to patients with mild ARDS (RR = 5.79; 95% CI, 3.10–11.05; p <0.0001). There were nine patients (6.3%, 9/142) with mild ARDS who still needed ventilator support in contrast to 207 patients who did not need ventilatory support despite moderate to severe ARDS (63.3%, 207/327) (Tables 10 and 11).

There were 24.5% (49/200) of diabetics who were on ventilator and 73.2% (230/314) of nondiabetics who were not on ventilator. The risk for the diabetics on the ventilator was 8% higher than the nondiabetics (RR = 0.92; 95% CI, 0.71–1.18; p = 0.603), which was not significant (Fig. 3).

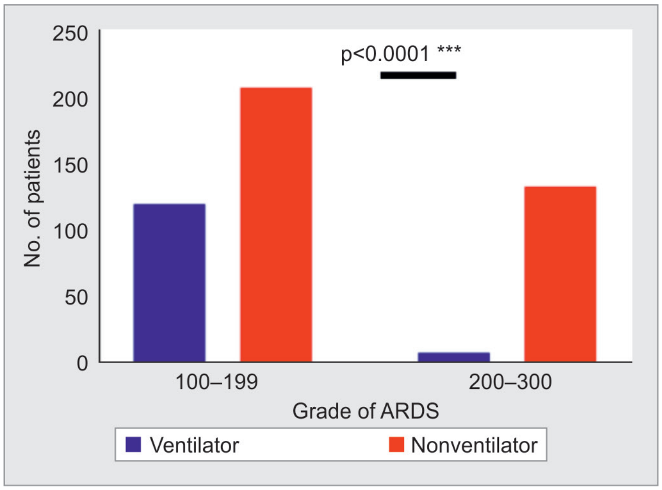

Fig. 2: Different oxygenation methods across the cohort with moderate-severe ARDS and mild ARDS

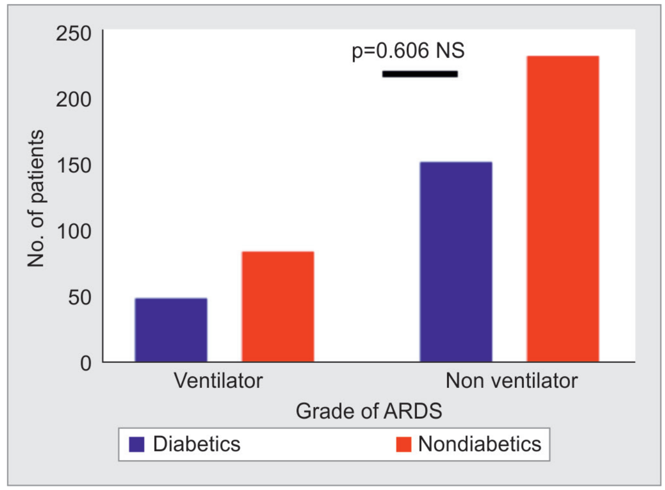

Fig. 3: Ventilator across diabetics and nondiabetics

Table 10: Distribution of grade of ARDS (P/F ratio) compared with the number of patients on ventilator

ARDS grade	*Number*
<100 (severe)	59
100–199 (moderate)	61
200–300 (mild)	9
>300 (no ARDS)	4
Total	133

Table 11: Number of patients on ventilator compared to the number of patients without ventilator support categorized across ARDS grade

Grade of ARDS	*No of patients on ventilator*	*No of patients not on ventilator*	*Total*
<100 (severe)	59	10	69
100–199 (moderate)	61	197	258
200–300 (mild)	9	133	142
>300 (no ARDS)	4	41	45
	133	381	514

Prone Ventilation

In patients on invasive ventilation, the prone ventilation strategy was used in 92.85% of patients. On patients with HFNC, the awake prone strategy was used in 96% of patients (Table 12).

The mean hours of prone ventilation was 17 hours for each ventilated patient. Prone ventilation was universally adopted if the P/F ratio remained low below 100 or worsening the respiratory mechanics.

Invasive Ventilation

A total of 133 (25.8%) patients were ventilated, and 44.3% ($n = 59$) were with severe ARDS. Among ventilated patients, 42.8% ($n = 57$) underwent percutaneous tracheostomy and 36.8% ($n = 49$) were extubated. The percentage of mortality in ventilated patients was 25.56% ($n = 34$).

Table 12: Prone ventilation with different modes of oxygenation

Row labels	*Awake prone*	*Prone*	*Nil*	*Total*
HFNC	235		8	243
Ventilator		118	15	133
NP	67		18	85
NIV	11		10	21
NRBM	13		1	14
RA	7		6	13
FM	1			1
ECMO			1	1
	334	118	59	511

No of ICU Days in Patients on Ventilator

The mean number of days in ICU in patients on ventilator was 12 (±6, minimum, 1; maximum, 30; range, 29; 95% CI, 11–13; $p = 0.613$ NS). The mean number of days on ventilator was 9.2 (±5.5, minimum, 1; maximum, 25; range, 24; 95% CI, 8.5–9.9; $p = 0.613$ NS)

The mean percentage of ICU days on ventilator was 77 (±23, minimum, 17; maximum, 100; range, 83; 95% CI, 73–81). The risk for mortality on ventilator was independent of the number of days on ventilator ($p = 0.63$). Numerically, the patients who died were for relatively less number of days on ventilatory support (mean, 7.7 days) as compared to the mean number of days who were discharged (9.7 days) (Fig. 4).

The risk for death was six times higher for the patients on the ventilator as compared to those who were not on ventilator (RR= 6.08; 95% CI, 3.49–10.59; $p < 0.0001$). There were 68% ($n = 34$) of the patients on the ventilator who died as compared to 78.6% ($n = 365$) who were discharged and were not on ventilator. And 24.8% ($n = 34$) of the patients on ventilator ($n = 133$) eventually died (Table 13).

There were a greater number of patients who did not require the support of mechanical ventilation ($n = 381$, 74.1%). The difference in the ICU days in patients on ventilator support (mean, 12 days) was statistically significant ($p < 0.0001$) as compared to patients who did not require ventilatory support while in the ICU (mean, 6.5 days) (Fig. 5).

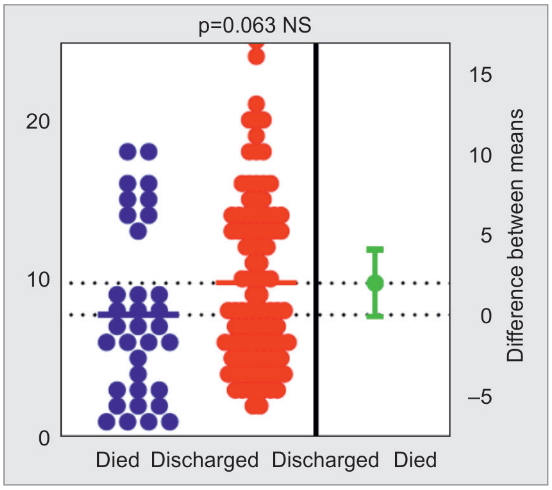

Fig. 4: Comparison of the mortality based on the number of days on the ventilator

Table 13: Number of patients on ventilator compared to the number of patients without ventilator support categorized across the mortality

	Died	*Discharged*	*Total*
Ventilator	34	99	133
Nonventilator	16	365	381
Total	50	464	514

Number of patients on ventilator compared to the number of patients without ventilator support categorized across the number of days in ICU

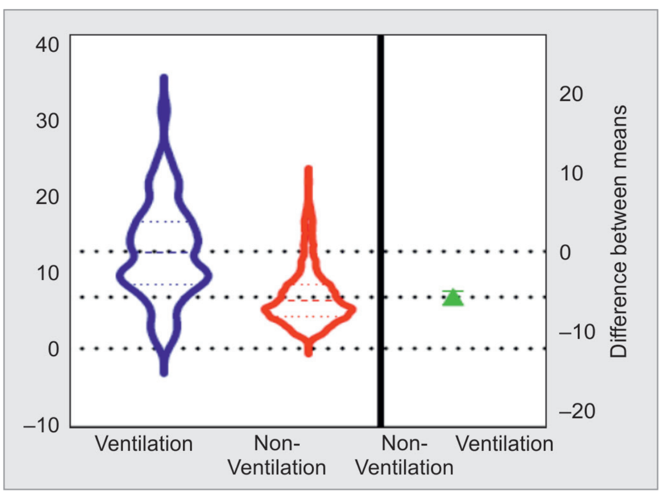

Fig. 5: Difference in ICU days of the patients on ventilator support

Table 14: Course among ventilated patients ($n = 133$)

Method	*n (%)*
Tracheostomy	57 (42.85)
Extubation	49 (36.8)
Death on ventilator	34 (25.56)

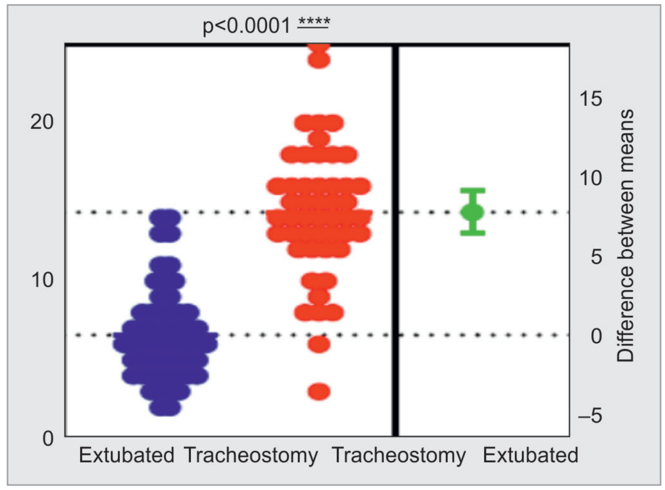

Fig. 6: Course among ventilated patients

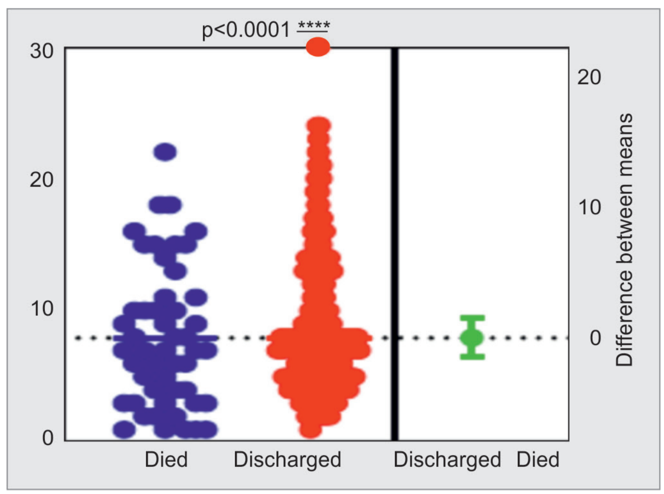

Fig. 7: Difference between the number of days on ventilator and tracheostomy

There was a statistically significant greater number of days the patients were on ventilator who underwent tracheostomy ($n = 49$, mean 14 days) as compared to the number of patients who underwent intubation ($n = 57$; mean, 6.4 days), ($p < 0.0001$) (Table 14; Fig. 6).

The patients who required 14 days of ventilatory support had higher chances of tracheostomy (Fig. 7).

Steroids

There were 9.53% ($n = 49$) of patients who did not receive steroids because of contraindications, and steroids were avoided in pregnant patients. Intravenous methylprednisolone (MPS) in a dosage of 0.5–2 mg/kg was used in 98.4% ($n = 458$) of patients who received steroid ($n = 465$). Twelve patients (24.4%) died who did not receive steroids.

Tocilizumab (TCZ)

A recombinant monoclonal antibody acting as IL-6 receptor inhibitor was one of the medications to use for cytokine storm in COVID-19 infection. Ninety-six patients out of 514 (18.6%) received TCZ. In our study, 9.09 (8/88)% of mortality was observed in TCZ group.

Antiviral

Two-hundred and sixty-five (51.5%) patients received antiviral drugs, of which two-hundred and forty received remdesivir, 18 patients received favipiravir, and 7 received the combination of lopinavir and ritonavir.

Duration of Stay

The mean duration of ICU stay (days) was 8 (±5, minimum, 1; maximum, 30; range, 29; 95% CI, 7.5–8.4).

Thromboprophylaxis

All patients except two admitted with intracranial hemorrhage were given thromboprophylaxis as enoxaparin 40 mg subcutaneously daily, and in patients with d-dimer level higher than two times the normal limit, the dose was increased to twice daily. In patients who had documented arterial or venous thrombosis they received 1 mg/kg body weight enoxaparin twice daily.

Mortality

Fifty patients expired (9.72%), and the rest recovered and discharged.

Mortality was based on the number of ICU days. The number of ICU days did not have any bearing on mortality. The duration of ICU stay was comparable irrespective of whether the patient died (mean, 7.9 days) or discharged (mean, 8 days; $p = 0.97$ NS). The longest duration of 30 days was in the patient who was discharged as compared to 22 days of ICU stay in the patient who died (Fig. 8).

Itolizumab

There were eight patients; none expired, and six who were on ventilator were discharged. None of the eight patients expired. Six patients required ventilatory support.

P/F ratio was negatively correlated with the number of days of hospitalization (Pearson's *r*, −0.391; 95% CI, −0.46 to −0.31; $p < 0.0001$) (Flowchart 1).

There were 67% of less chances of mortality in patients on steroids (RR = 0.33; 95% CI, 0.19–60; $p = 0.0012$) (Table 15).

There was an insignificant 10% reduction in risk of mortality in patients who were on TCZ (RR = 0.90; 95% CI, 0.44–1.7; $p = >0.9999$ NS) (Table 16).

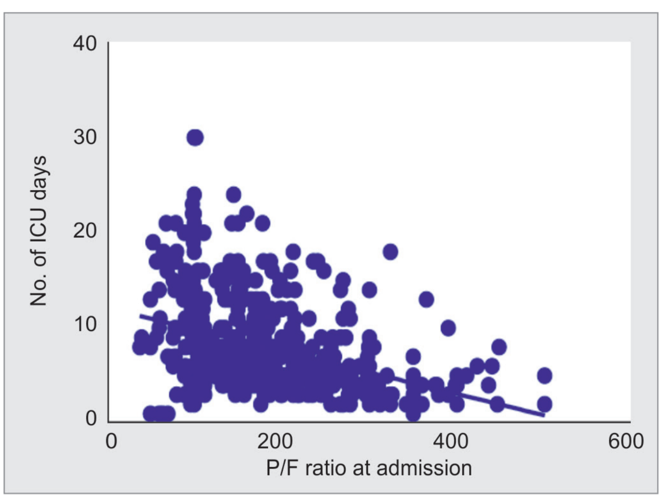

Fig. 8: Difference between the mortality and the number of days in ICU

Flowchart 1: Simple linear regression of correlation between P/F ratio and ICU days

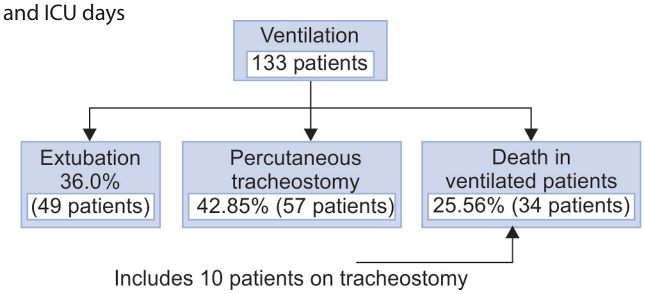

Table 15: Mortality based on the usage of steroids

	Died	*Discharged*	*Total*
Steroids	38	427	465
Nonsteroids	12	37	49
Total	50	464	514

Table 16: Mortality based on the usage of TCZ

	Died	*Discharged*	*Total*
TCZ	8	80	88
No TCZ	42	376	418
Total	50	456	506

Table 17: Mortality based on the usage of antivirals

	Died	*Discharged*	*Total*
Antiviral	16	249	265
No antiviral	34	215	249
Total	50	464	514

There was a significant 56% reduction in death in patients who were on antivirals (RR = 0.44; 95% CI, 0.25–0.77; $p = 0.0044$) (Table 17).

Discussion

In a meta-analysis conducted by Abate and et al., the rate of ICU admission with COVID-19 infection was found to be 32%.[6] Guan and colleagues reported that patients presenting with COVID-19 infection had varied symptoms, from mild fever, cough, or gastrointestinal manifestation to severe respiratory distress leading to respiratory failure and mortality.[7] The severity of the infection had a significant correlation with age and preexisting comorbid conditions. Triage of these cases depending on the severity helped the healthcare system to combat the epidemic outbreak amidst the crises. The patients with respiratory distress, hypoxia with or without preexisting medical conditions, accounted for a major part of the ICU admission.[8]

We postulate that the reason for young males being the highest proportion being admitted to ICU could be for the younger males would be out in the community as unlocking happened as they are generally the primary breadwinner of the family and the livelihood after a long lockdown necessitated them to move out to work. Consequently, that exposed them to SARS-CoV-2 in higher numbers. Similarly, the lower number of community exposures for the elderly could have resulted in relatively lower ICU admissions. The patients who required 14 days of ventilatory support had higher chances of tracheostomy. The mortality outcomes were independent of the number of days the patient has been in the ICU. The appropriate utilization of steroids appears to be a useful modality to improve the mortality outcomes. The appropriate utilization of antivirals appears to be a useful modality to improve the mortality outcomes. TCZ is not useful for improving mortality benefits.

In our analysis, 514 patients with COVID-19 infection were observed in both young and elder patients. The retrospective study by Sun et al. from China found that people above 60 years of age were most affected with the highest case fatality.[8] Gebhard et al. found that both men and women were equally suspectable to COVID-19 infection,[9] whereas a study of 140 patients from China found that the incidence of infection was 67% among men.[10] The higher risk of severe illness and fatality among men due to the disease was explained by multiple theories.[11] Biological theory proposed for this was based on genomics, X chromosome, which has more genes for immune regulation and immune response to infection.[12] Women with XX chromosome, double copy of immune genes, might tackle the coronavirus infection effectively.[13] All studies and meta-analysis published on the severity of COVID-19 pneumonia and its association with other preexisting medical conditions prove that the case fatality and severity were more in these patients.[7] Diabetes causes a dysregulated immune response to infection and makes the person more vulnerable. Plasma glucose levels and diabetes were found to be the independent predictor for mortality and morbidity.[14] The incidence of diabetes among 514 COVID-19 patients was higher of 38.9% (n = 200), than the other studies and was highest in comparison with other coexisting conditions. On subgroup analysis, the requirement of ventilatory support was found to be 24.5% among diabetic patients.

Patients with systemic hypertension were at higher risk of COVID-19 infection-related mortality.[15] The incidence of hypertension in our analysis was 31.6%, which was second to diabetes. Whereas in a meta-analysis of eight trials that included 46,248 COVID-19 patients, Yang et al. reported a prevalence of 17, 8, and 5% for hypertension, diabetes, and CVD, respectively.[16] We attribute for the higher mortality in these patients for greater incidence of hypertension in elders. The drugs used in treatment of hypertension, ACE inhibitors and ARBs were proposed theoretically to increase the viral binding in lungs and responsible for severity. However, the effects of ACE inhibitors remain in-conclusive.[17]

Cardiovascular manifestations were not uncommon in COVID-19 infection. The prevalence of infection-related CVD in our analysis was 10.9%. Patients with a history of ischemic heart disease had a higher incidence of infections, accounting for 85.1% of CVD. In a systemic meta-analysis, 22% of patients were admitted with acute myocardial injury to ICU.[18] In our study, the acute coronary event was documented in three patients on admission to COVID-19 ICU, which was attributed to inflammation, increase in metabolic demands, and arrhythmias in COVID-19 infection.[19] Patients with chronic lung diseases were found to have a higher incidence of infection. In a multicentric observational study, patients with chronic obstructive pulmonary disease (COPD) had higher incidence of ICU admission.[20] According to our analysis, the incidence of pulmonary disease among our patients was 3.7%, and this includes patients with COPD, bronchial asthma, and two patients with pulmonary tuberculosis.

Immunosuppression among CKD and postrenal transplant may result in an increased incidence of COVID-19 infection. The prevalence of COVID-19 infection among CKD patients was found to be 5.2%, which included three patients of postrenal transplant, one with pyelonephritis, and one patient presented with acute kidney injury. The publication from the Oxford University states that the CKD patients had three-fold higher risk of COVID-19 infection.[21]

Hypoxia and respiratory distress were being the most common cause for ICU admission.[8] Analysis of arterial oxygen levels guides the oxygen therapy and classifies the ARDS into mild, moderate, and severe. In our study, the mean P/F ratio was found to be 185. In a study of 1,740 patients with ICU admission, a large number of patients required advanced oxygen support.[22] The low P/F ratios, along with other factors, are now being attributed as pathophysiological reflection for the mechanism of hypoxia. The low P/F ratios may imply a process occurring on the vascular side of the alveolar-capillary unit.[23]

Oxygen methods used were nasal prongs, high flow nasal oxygenation (HFNC), NIV, and invasive ventilator support. In our study, high flow nasal oxygenation was found to be the highest, followed by invasive ventilation and nasal prongs, respectively. The success rate of HFNC was found to be 83% in our study, in avoiding patients from going on ventilator.

Recruitment of lung parenchyma by prone ventilation in severe ARDS has a proven benefit that was well documented in the PROSEVA trial.[24] Awake prone ventilation among COVID-19 patients is one of the strategies to improve oxygenation. A cohort study of 54 patients concluded that the prone positioning was effective and ameliorates blood oxygenation in awake patients.[25] A recent study has demonstrated the substantial efficacy of the prone position.[26] In our study, awake prone was used in 96% of patients, and prone ventilation was used in all patients on mechanical ventilation except in patients with morbid obesity, acute stroke, thrombosis of limbs, and pregnancy.

Percutaneous tracheostomy was done in the patients with prolonged ventilation. Avoiding aerosol production during tracheostomy imposed a unique challenge to clinicians. The percutaneous tracheostomy method in COVID-19 has undergone minimal modification in the form of maintaining apnea during dilatation, with a significant reduction in aerosol production with good success and without an increase in complications.

In our study, 93.1% of patients with severe ARDS received invasive ventilation, and 42.85% of patients required percutaneous tracheostomy.

In our study, only 9.53% (n = 49) of patients did not receive steroids because of contraindications, and steroids were avoided in pregnant patients. MPS was used in 98.4% of patients who received steroids. Twelve patients (24.4%) died who did not receive steroids. RECOVERY trial documents that the use of dexamethasone in COVID-19 patients reduces the 28-day mortality and also proves that the incidence of death was less in the invasive mechanical ventilation group.[27]

We attribute prone position as part of good ARDS management practice that contributed to improved outcomes, adding to the existing evidence base for the distinctive improved outcomes.

Appropriate NIV or HFNC was the other best measures adopted consistently, which would also be attributed for improved outcomes.

In our study, the overall ICU mortality was 10.15%, which was lesser compared to other studies.[6,22] A recent meta-analysis across

33 studies with a total of 13,398 patients suggests a mortality rate of 17.1%. Among critical illness studies across seven studies, the mortality rate has been found to be as high as 40.5%. The mortality among diabetic patients was found to be higher, which was similar to other studies.[14,15,28] Death among ventilated patients was lesser compared to other studies.[27,29] TCZ group also had a mortality of 10%.

Attributes that would Account for Better Outcomes in Our Set-up

The best infection control practices have been followed for several years that has led to low secondary infections. Our institution was conferred the prestigious British Medical Journal (BMJ) Award for 'The Medical Team of the Year 2014.' The honor was bestowed on the hospital for its outstanding 'antibiotic review program and antibiotic restriction policy'. Although, we operate in an ecosystem with limited resources, the administration and the logistics support provided to us was exceedingly timely that enabled the quality utilization of the best of manpower capabilities. The human manpower across the entire spectrum including the paramedical support to the consultants were well trained with high degree of empowered approach for a quick decision making and rapid implementation of the skills. This contributed well qualitatively to the better outcomes. We have been adherent to the global standard care like adhering to ARDS net protocol and pronation.

Logistics support has been a challenge during the time of unanticipated crisis. The management of our institution was supportive and pragmatic to enable an appropriate rooster allocation that mitigated the burn out phenomenon and yet kept the staff motivated to the highest degree to deliver best of the human capabilities, minimizing the errors in the implementation of the clinical decision-making process. Importantly, the senior most team was directly involved on the floor care. All clinical staff led from front which enabled a consistent high degree of motivation and delivered the efficient care.

Our institution, being a tertiary care center, serves well to the local community and hence the patients can reach the hospital relatively early. Inherently, we realize that overall, the treatment had been started relatively much early in the disease process. That is an important contributing reason for better outcomes. The early presentation also enabled a judicious decision making at an appropriate time, which is one of the important reasons for the timely intubation, while utilizing the best of the available resources. The reason for the early presentation is attributed to the better physician awareness in the metropolitan area. Also, our institution is actively involved in the outreach programs catering to both clinician and patient education and awareness. We attribute these as important, factors that have contributed for a timely referral of the patients to our hospital.

We were not able to conduct genomic studies. Hence, we do not know if, relatively less mortality be attributed to a particular strain of virus. However, this is an area of further exploration.

Conclusion

In a study of 514 patients admitted to a tertiary care ICU, the most common reason for admission was hypoxia. We attribute that the relatively less mortality in ICU setting due to strict adherence to the basic proven principles of ARDS management was observed. Measures like following ARDS net recommendations for ventilation, prone ventilation, low dose steroids, thromboprophylaxis, and the use of HFNC perhaps proved to be beneficial. The role of novel agents like IL-6 receptor blockers needs to be further studied as it is associated with a higher incidence of hospital-acquired infection. The overall mortality in our ICU patients was 10.15% and in ventilated patients was 25.7% much lower than other reported studies.

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References

1. Chalmers JD, Crichton ML, Goeminne PC, Cao B, Humbert M, Shteinberg M, et al. Management of hospitalised adults with coronavirus disease-19 (COVID-19): a European Respiratory Society living guideline. Eur Respir J 2021;57(4):2100048. DOI: 10.1183/13993003.00048-2021.
2. Sarma P, Bhattacharyya A, Kaur H, Prajapat M, Prakash A, Kumar S, et al. Efficacy and safety of steroid therapy in COVID-19: A rapid systematic review and Meta-analysis. Indian J Pharmacol 2020;52(6):535–550. DOI: 10.4103/ijp.ijp_1146_20.
3. Zhan Y, Shang J, Gu Y, Huang Q, Xie J. Efficacy of corticosteroid in patients with COVID-19: a multi-center retrospective study and meta-analysis. J Med Virol 2021;93(7):4292–4302. DOI: 10.1002/jmv.26914.
4. Macedo A, Gonçalves N, Febra C. COVID-19 fatality rates in hospitalized patients: systematic review and meta-analysis. Ann Epidemiol 2021;57:14–21. DOI: 10.1016/j.annepidem.2021.02.012.
5. ARDS Definition Task Force, Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, et al. Acute respiratory distress syndrome: the Berlin definition. JAMA 2012;307(23):2526–2533. DOI: 10.1001/jama.2012.5669.
6. Abate SM, Ahmed Ali S, Mantfardo B, Basu B. Rate of Intensive Care Unit admission and outcomes among patients with coronavirus: a systematic review and meta-analysis. PLoS One 2020;15(7):e0235653. DOI: 10.1371/journal.pone.0235653.
7. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382(18):1708–1720. DOI: 10.1056/NEJMoa2002032.
8. Sun H, Ning R, Tao Y, Yu C, Deng X, Zhao C, et al. Risk factors for mortality in 244 older adults with COVID-19 in Wuhan, China: a retrospective study. J Am Geriatr Soc 2020;68(6):E19–E23. DOI: 10.1111/jgs.16533.
9. Gebhard C, Regitz-Zagrosek V, Neuhauser HK, Morgan R, Klein SL. Impact of sex and gender on COVID-19 outcomes in Europe. Biol Sex Differ 2020;11(1):1–3. DOI: 10.1186/s13293-020-00304-9.
10. Jj Z, Dong X, Yd Y, Yq Y. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. Allergy 2020;75(7):1730–1741. DOI: 10.1111/all.14238.
11. Yang X, Yu Y, Xu J. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med 2020;8(5):P475–P481. DOI: 10.1016/S2213-2600(20)30079-5.
12. Gemmati D, Bramanti B, Serino ML, Secchiero P, Zauli G, Tisato V. COVID-19 and individual genetic susceptibility/receptivity: role of ACE1/ACE2 genes, immunity, inflammation and coagulation. Might the double X-chromosome in females be protective against SARS-CoV-2 compared to the single X-chromosome in males? Int J Mol Sci 2020;21(10):3474. DOI: 10.3390/ijms21103474.

13. Olds JL, Kabbani N. Is nicotine exposure linked to cardiopulmonary vulnerability to COVID-19 in the general population? FEBS J 2020 [in press]. DOI: 10.1111/febs.15303.
14. Singh AK, Gupta R, Ghosh A, Misra A. Diabetes in COVID-19: Prevalence, pathophysiology, prognosis and practical considerations. Diabetes Metab Syndr 2020;14(4):303–310. DOI: 10.1016/j.dsx.2020.04.004.
15. Muniyappa R, Gubbi S. COVID-19 pandemic, coronaviruses, and diabetes mellitus. Am J Physiol Endocrinol Metab 2020;318(5): E736–E741. DOI: 10.1152/ajpendo.00124.2020.
16. Yang J, Zheng Y, Gou X, Pu K, Chen Z, Guo Q. Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: a systematic review and meta-analysis. Int J Infect Dis 2020;12. DOI: 10.1016/j.ijid.2020.03.017. PII: S1201-9712(20)30136-3.
17. Turner JM, Kodali R. Should angiotensin-converting enzyme inhibitors ever be used for the management of hypertension? Curr Cardiol Rep 2020;22(9):95. DOI: 10.1007/s11886-020-01352-8.
18. Long B, Brady WJ, Koyfman A, Gottlieb M. Cardiovascular complications in COVID-19. Am J Emerg Med 2020;38(7):1504–1507. DOI: 10.1007/s11886-020-01352-8. PMID: 32648000; PMCID: PMC7344347.
19. Lazaridis C, Vlachogiannis NI, Bakogiannis C, Spyridopoulos I, Stamatelopoulos K, Kanakakis I, et al. Involvement of cardiovascular system as the critical point in coronavirus disease 2019 (COVID-19) prognosis and recovery. Hellenic J Cardiol 2020;61(6):381–395. DOI: 10.1016/j.hjc.2020.05.004.
20. Wu F, Zhou Y, Wang Z, Xie M, Shi Z, Tang Z, et al. Clinical characteristics of COVID-19 infection in chronic obstructive pulmonary disease: a multicenter, retrospective, observational study. J Thorac Dis 2020;12(5):1811. DOI: 10.21037/jtd-20-1914. PMID: 32642086; PMCID: PMC7330323.
21. D'Marco L, Puchades MJ, Romero-Parra M, Gimenez-Civera E, Soler MJ, Ortiz A, et al. Coronavirus disease 2019 in chronic kidney disease. Clin Kidney J 2020;13(3):297–306. DOI: 10.1093/ckj/sfaa104. PMID: 32699615; PMCID: PMC7367105.
22. Armstrong RA, Kane AD, Cook TM. Outcomes from intensive care in patients with COVID-19: a systematic review and meta-analysis of observational studies. Anaesthesia 2020;75(10):1340–1349. DOI: 10.1111/anae.15201.
23. Nitsure M, Sarangi B, Shankar GH, Reddy VS, Walimbe A, Sharma V, et al. Mechanisms of hypoxia in COVID-19 patients: a pathophysiologic reflection. Indian J Crit Care Med 2020;24(10):967–970. DOI: 10.5005/jp-journals-10071-23547.
24. Guérin C, Reignier J, Richard JC, Beuret P, Gacouin A, Boulain T, et al. Prone positioning in severe acute respiratory distress syndrome. N Engl J Med 2013;368(23):2159–2168. DOI: 10.1056/NEJMoa1214103.
25. Coppo A, Bellani G, Winterton D, Di Pierro M, Soria A, Faverio P, et al. Feasibility and physiological effects of prone positioning in non-intubated patients with acute respiratory failure due to COVID-19 (PRON-COVID): a prospective cohort study. Lancet Respir Med 2020;8(8):765–774. DOI: 10.1016/S2213-2600(20)30268-X. PMID: 32569585; PMCID: PMC7304954.
26. Simioli F, Annunziata A, Langella G, Martino M, Musella S, Fiorentino G. Early prone positioning and non-invasive ventilation in a critical COVID-19 subset. a single centre experience in Southern Italy. Turk Thorac J 2021;22(1):57–61. DOI: 10.5152/TurkThoracJ.2021.20158.
27. Docherty AB, Harrison EM, Green CA, Hardwick HE, Pius R, Norman L, et al. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. BMJ 2020;369:m1985. DOI: 10.1136/bmj.m1985.
28. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. JAMA 2020;323(20):2052–2059. DOI: 10.1001/jama.2020.6775.
29. Huang I, Lim MA, Pranata R. Diabetes mellitus is associated with increased mortality and severity of disease in COVID-19 pneumonia – a systematic review, meta-analysis, and meta-regression. Diabetes Metab Syndr 2020;14(4):395–403. DOI: 10.1016/j.dsx.2020.04.018.