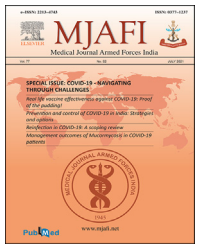
Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/mjafi



Original Article

Characteristics, therapeutic modalities and outcomes of COVID-19 ventilated patients in a tertiary care hospital in counter-insurgency zone: Our experience

Parikshit Singh [a,*], *S.K. Singh* [b], *Yadvir Garg* [c], *D.J. Gajbhiye* [d], *A.K. Jindal* [e], *Kavita Sahai* [f]

[a] *Senior Advisor & Critical Care Specialist (Anaesthesiology & Critical Care), Command Hospital (Northern Command), Udhampur, India*
[b] *Classified Specialist (Medicine), Command Hospital (Northern Command), Udhampur, India*
[c] *Classified Specialist (Pulmonary Medicine), Command Hospital (Northern Command), Udhampur, India*
[d] *Classified Specialist (Anaesthesiology & Critical Care), Command Hospital (Northern Command), Udhampur, India*
[e] *Commandant, Command Hospital (Northern Command), Udhampur, India*
[f] *Deputy Commandant & Consultant (Pathology), Command Hospital (Northern Command), Udhampur, India*

ARTICLE INFO

Article history:
Received 20 May 2021
Accepted 18 June 2021

Keywords:
COVID-19
Ventilated patient characteristics
Therapies
Outcomes

ABSTRACT

Background: Coronavirus disease 2019 (COVID-19) can result in severe life-threatening course requiring ventilatory support. This study highlights data pertaining to ventilated patients to enhance our understanding of COVID-19 as it evolves.
Methods: A descriptive, retrospective analysis was carried out on 50 COVID-19 RT-PCR positive patients who received mechanical ventilation at a tertiary care hospital in counter-insurgency (CI) zone, from June to December 2020. Data pertaining to patient characteristics, treatment, ventilator support and outcomes was analysed.
Results: Out of 50 patients, 74% were aged 50 years and above with 60% patients having comorbidities. 39 patients received non-invasive ventilation (NIV) and 04 patients received invasive mechanical ventilation (IMV) while 07 patients were converted from NIV to IMV during the hospital stay. Out of the 50 patients who received ventilator support 25 (50%) survived to discharge. The overall survival was 47.3% amongst the males while it was 58.3% for the females. The majority of survivors were in the NIV category (61.5%) while only 9.0% survived amongst those who received IMV. Average length of stay on NIV for patients was 5.3 days and for IMV was 7.5 days. All 50 patients received therapy in the form of steroids, anticoagulants, broad spectrum antibiotics and antivirals. Remdesivir was given to 40 of these patients out of which 20 survived (50%). Interleukin-6 therapy (Tocilizumab) was given to five patients of which four survived (80%).

* *Corresponding author.*
E-mail address: drparikshitsingh@yahoo.co.in (P. Singh).
https://doi.org/10.1016/j.mjafi.2021.06.023

Conclusion: This study helps us to gain insights into the outcomes of COVID-19 patients managed in a tertiary care hospital in CI zone.

Introduction

The rapid outbreak of coronavirus disease 2019 (COVID-19), which arose from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, has become a public health emergency of international concern from November 2019.[1] Infection by COVID-19 can result in a range of clinical outcomes, from asymptomatic to severe life-threatening course or death. Characterization of epidemiological, clinical, comorbid features with recovery and mortality of COVID-19 is crucial for development and implementation of effective control strategies and management protocol.[2] It is also equally important to get insights into the characteristics and outcomes of patients being ventilated be it with Non Invasive Ventilation (NIV) or Invasive Mechanical Ventilation (IMV).

Based on current epidemiological investigation, the incubation period of COVID-19 seems to be 1–14 days, mostly 3–7 days. COVID-19 is contagious during its latency period.[2] It is known to be highly transmissible in humans, especially in the elderly and people with underlying diseases. The clinical manifestations of COVID-19 are heterogeneous with fever, cough, sore throat, shortness of breath, headache and fatigue being the predominant features.[3] On admission, many patients have reported as having at least one comorbidity with diabetes, hypertension, and cardiovascular and cerebrovascular diseases being most commonly reported conditions.[4] As opposed to the common practice of pursuing IMV for all severe COVID-19 pneumonia patients in the earlier part of the pandemic a trend towards NIV started towards the middle of the first wave with better outcomes.[5]

COVID-19 was declared a public health emergency of pandemic proportions and subsequently formal screening and diagnostic investigations for SARS-CoV-2 was initiated throughout India. This study highlights our experience pertaining to the characteristics and therapies deployed in the critically ill COVID-19 patients who were mechanically ventilated at our hospital and their final outcomes.

Material and methods

The present descriptive, retrospective analysis was done on 50 COVID-19 reverse transcription polymerase chain reaction (RT-PCR) positive patients who required ventilatory support at a tertiary care hospital, in a counter-insurgency (CI) zone, from June to December 2020 during the first wave of the pandemic. The privacy and confidentiality of patients was observed as per norms.

After collection of all required data and careful medical chart review, the clinical data of laboratory-confirmed 50 hospitalized patients over a 07 month period was compiled and tabulated. The diagnosis of COVID-19 was made based on the World Health Organization interim guidance, wherein confirmed cases denoted were patients whose RT-PCR assay findings for nasal and pharyngeal swab specimens were positive. The epidemiological data (age, sex and body mass index) was noted apart from clinical data inclusive of co-morbidities, computed tomography (CT) severity, the type of mechanical ventilation given (NIV or IMV) with the basic ventilator settings, the days spent on ventilator and the final outcome. Also recorded were the therapeutic interventions made in all these like the use of steroids, antivirals, low molecular weight heparin (LMWH), Interleukin-6 (IL-6) therapy, antifibrotics and any additional antibiotics.

The CT severity score is mostly used to assess the lung changes caused by COVID-19 taking into account the lung lobar area involvement. Based on the radiologist's interpretation the total CT Severity Score (CT-SS) is categorised into mild (7 or less), moderate (8–17) and severe (18–25).[6] The same benchmark was used in our study. Body mass index (BMI) was calculated based on previously available weight-height records or as recalled by the patient or family members. Based on WHO classification, they were divided into underweight (BMI < 18.5 kg/m2), normal (BMI 18.5–24.9 kg/m2), overweight (BMI 25–29.9 kg/m2), obese (BMI 30–34.9 kg/m2), severely obese (BMI 35–39.9 kg/m2) and morbid obese (BMI $\geq$ 40 kg/m2).[7]

The primary endpoint of the study was a characterisation of COVID-19 ventilated patients who were treated at our hospital during the first wave of the pandemic and to look at their outcomes.

Results

A total of 50 ventilated patients of RT-PCR confirmed COVID-19 were studied at our hospital for baseline characteristics like age, sex, CT severity and BMI apart from the basic ventilator settings and the final outcomes (Table 1). Out of 50 patients, 74% were aged 50 years and above (N = 37), and the mean age was 57.84 years. The age ranges have been depicted in Fig. 1. 76% of patients were males (N = 38) while 24% were females (N = 12) as depicted in Fig. 2. The most prevalent co-morbidities were hypertension (HTN; 14/50) and type - 2 diabetes (Type-II DM; 9/50) followed by obesity (8/50), chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD) and coronary artery disease (CAD) as shown in Fig. 3. 60% patients had comorbid conditions.

Table 1 – Patient characteristics and ventilatory details.

S. No.	Age/Sex	CT Severity	BMI (Kg/m^2)	Type of Mechanical Ventilation & Total Days Spent		CARP/Proning	Max Ventilator Settings		Outcome
				NIV	IMV		NIV/(PS) (CPAP/FiO2)	IMV/(PC) (PEEP/FiO2)	
1.	38/F	Severe	Morbidly Obese	01	01	No	7/0.90	10/1.0	Expired
2.	50/M	Severe	Normal	09	27	Prone	8/0.80	14/0.9	Survived
3.	33/M	Mild	Normal	01	–	No	5/0.50	–	Survived
4.	25/M	Mild	Normal	06	–	No	6/0.55	–	Survived
5.	80/M	Mild	Underweight	01	–	No	5/0.80	–	Expired
6.	44/M	Moderate	Normal	04	–	CARP	6/0.60	–	Survived
7.	89/F	Mild	Underweight	03	–	No	5/0.65	–	Survived
8.	52/M	Moderate	Normal	–	08	No	–	8/1.0	Expired
9.	62/M	Moderate	Overweight	01	–	No	5/0.90	–	Expired
10.	59/M	Severe	Overweight	17	06	Prone	8/0.85	12/1.0	Expired
11.	37/M	Mild	Normal	13	–	CARP	7/0.80	–	Survived
12.	70/M	Severe	Overweight	03	–	No	6/0.95	–	Expired
13.	60/F	Severe	Obese	07	–	CARP	7/0.70	–	Survived
14.	65/M	Severe	Overweight	07	–	No	8/0.90	–	Expired
15.	78/M	Moderate	Normal	09	–	CARP	7/0.90		Expired
16.	70/M	CT not done	Overweight	–	04	No	–	8/1.0	Expired
17.	56/M	Moderate	Normal	05	–	CARP	6/0.60		Survived
18.	80/M	Mild	Normal	03	–	No	7/0.85		Expired
19.	85/M	CT not done	normal	01	–	No	5/0.75	–	Expired
20.	56/M	Severe	Normal	10	05	CARP	8/0.80	10/0.90	Expired
21.	61/M	Severe	Overweight	01	–	No	5/0.70	–	Expired
22.	57/M	Severe	Normal	12	09	Prone	7/0.85	12/1.0	Expired
23.	71/F	Mild	Morbidly obese	10	–	No	8/0.85	–	Expired
24.	55/M	Severe	Underweight	09	–	CARP	7/0.75	–	Survived
25.	53/F	Severe	Obese	05	–	No	6/0.80	–	Expired
26.	60/F	Mild	Obese	–	02	No	–	6/0.80	Expired
27.	80/M	Severe	Overweight	03	–	No	7/0.85	–	Expired
28.	66/M	Moderate	Normal	08	–	No	8/0.90	–	Expired
29.	65/M	Severe	Normal	–	13	Prone	–	14/1.0	Expired
30.	75/M	Severe	Normal	01	–	No	5/0.75	–	Expired
31.	75/M	Mild	Overweight	04	–	No	6/0.70	–	Expired
32.	57/M	Severe	Overweight	11	–	CARP	6/0.80	–	Survived
33.	61/F	Mild	Obese	04	–	No	5/0.40	–	Survived
34.	31/M	Severe	Normal	05	–	CARP	7/0.70	–	Survived
35.	71/M	Mild	Normal	02	–	No	5/0.40	–	Survived
36.	38/M	Severe	Overweight	02	–	CARP	5/0.50	–	Survived
37.	65/F	Severe	Overweight	07	–	–	7/0.75	–	Survived
38.	69/F	Severe	Normal	08	–	CARP	6/0.60	–	Survived
39.	53/M	Severe	Normal	08	–	–	6/0.70	–	Survived
40.	63/M	Severe	Morbidly Obese	10	–	–	8/0.85	–	Survived
41.	31/F	Severe	Normal	04	04	–	7/0.65	8/0.9	Expired
42.	66/M	Severe	Overweight	01	–	–	6/0.55	–	Survived
43.	66/M	Moderate	Normal	02	–	–	5/0.50	–	Survived
44.	41/F	Severe	Normal	02	–	CARP	6/0.55	–	Survived
45.	42/M	Severe	Normal	06	04	CARP	8/0.85	14/1.0	Expired
46.	45/M	Moderate	Normal	01	–	CARP	6/0.65	–	Survived
47.	39/M	Moderate	Normal	03	–	CARP	5/0.50	–	Survived
48.	63/M	Severe	Normal	08	–	CARP	7/0.80	–	Expired
49.	60/F	Moderate	Obese	02		–	6/0.70	–	Survived
50.	24/M	Severe	Normal	04	–	CARP	6/0.65	–	Survived

These 50 patients underwent ventilatory support over a period of 07 months from June 2020 to Dec 2020 with a majority of ventilation occurring in the 03 months from Sep to Nov 2020. Of these, 39 patients received purely NIV with pressure support (PS) and continuous positive airway pressure (CPAP) via a NIV facemask, and only 04 patients received pure IMV from the outset with pressure control (PC) and positive end expiratory pressure (PEEP) via an endotracheal tube. Covid Awake Repositioning Proning Protocol (CARP) while on NIV and prone ventilation while on IMV were undertaken where feasible. There were seven cases which received NIV to start with but were later converted to IMV. Hence, a total of 11 patients (04 + 07) ended up receiving IMV. This is depicted in Fig. 4.

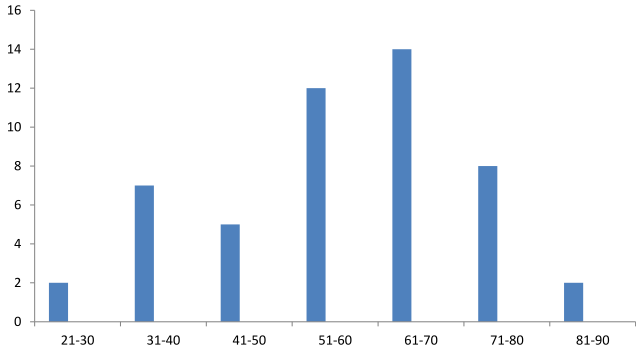


Fig. 1 – Age distribution (Years).

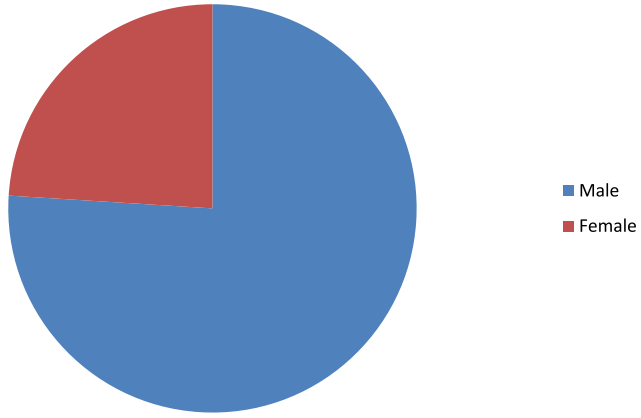


Fig. 2 – Gender distribution.

Out of all these 50 patients 25 survived to discharge. The overall survival was 47.3% amongst the male patients (18 out of 38) while it was 58.3% for the female patients (7 out of 12). The majority of survivors were in the NIV category with 24 surviving out of 39 patients (61.5%). Only one patient survived out of the 11 who received IMV (9.0%). The mechanical ventilation outcomes are depicted in Fig. 5.

The shortest stay on ventilator was 01 day for both NIV and IMV (both resulting in non-favourable outcomes) while the longest duration for NIV and IMV was 13 days and 27 days respectively (both resulting in favourable outcomes). The average length of stay on NIV for patients was 5.3 days and for IMV was 7.5 days. The overall average length of stay on ventilator (for both NIV + IMV combined) was 6.1 days. Out of total 39 patients on NIV, 17 received CARP protocol out of which 14 patients survived. 04 patients of IMV received prone ventilation out of which only 01 survived. 03 of these proned patients of IMV initially also received CARP while on NIV.

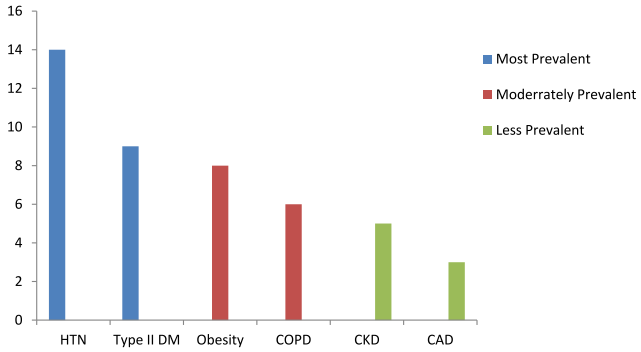


Fig. 3 – Prevalent comorbidities.

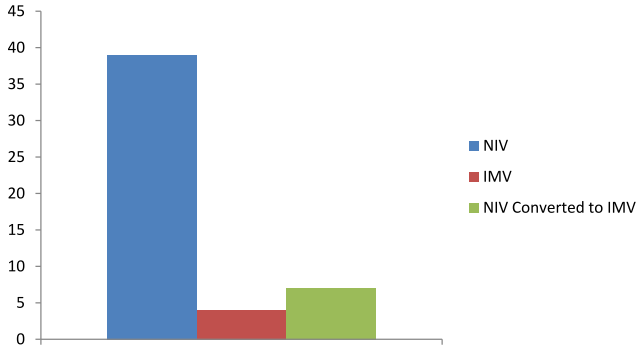


Fig. 4 – Types of ventilation administered.

All patients on NIV received an optimal setting combining PS, CPAP and Fraction of Oxygen in the Inspired Air (FiO2). The maximum CPAP and FiO2 combination received on NIV by a survivor was 8 and 0.85 respectively while in a non-survivor was 8 and 0.90. The minimum settings of CPAP/FiO2 for a survivor on NIV was 5 and 0.50 while for a non-survivor was 5 and 0.70. On the other hand the maximum PEEP and FiO2 settings on IMV for a survivor was 14 and 0.90 and for a non-survivor was 14 and 1.0. The lung protective strategy of low tidal volumes, optimal PEEP and keeping plateau pressures less than 30 cm H2O was followed in all IMV cases along with judicious use of sedation and also muscle relaxants where needed.

Therapeutic modalities used in management of these ventilated patients essentially included steroids, antivirals, anticoagulants, broad spectrum antibiotics and in a few cases, where applicable, IL-6 therapy as well as antifibrotics (Table 2).

As per treatment protocol all of our patients were given anti-viral therapy. All 50 patients were given Ivermectin (12 mg OD for 03 days) as per our institutional practice while 08 of the patients were given Favipiravir in the initial period. Remdesevir was administered to 40 patients who exhibited moderate to severe COVID-19 manifestations out of which 20 patients (50%) ultimately survived.

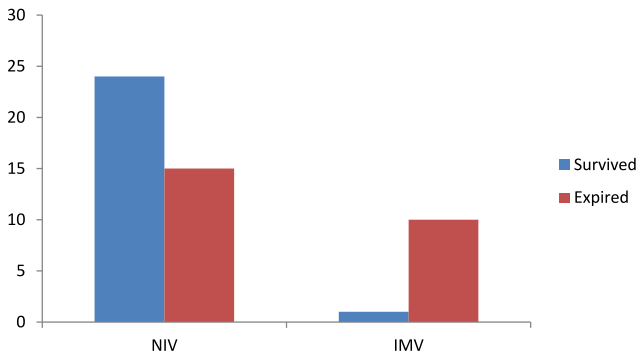


Fig. 5 – Final outcomes of ventilated patients.

Table 2 – Therapeutic modalities of ventilated patients.

S. No.	Age/Sex	CT Severity	Steroids	Antivirals			LMWH	Additional antibiotics	Outcome
				Ivermectin	Remdesivir	Favipiravir			
1.	38/F	Severe	Received by	√	√	-	Received by	Received by	Expired
2.	50/M	Severe	all patients	√	√	√	all patients	all patients	Survived
3.	33/M	Mild		√	-	-			Survived
4.	25/M	Mild		√	√	√			Survived
5.	80/M	Mild		√	-	-			Expired
6.	44/M	Moderate		√	√	√			Survived
7.	89/F	Mild		√	√	-			Survived
8.	52/M	Moderate		√	√	-			Expired
9.	62/M	Moderate		√	-	√			Expired
10.	59/M	Severe		√	√	√			Expired
11.	37/M	Mild		√	√	√			Survived
12.	70/M	Severe		√	√	√			Expired
13.	60/F	Severe		√	√	√			Survived
14.	65/M	Severe		√	√	-			Expired
15.	78/M	Moderate		√	√	-			Expired
16.	70/M	CT not done		√	√	-			Expired
17.	56/M	Moderate		√	√	-			Survived
18.	80/M	Mild		√	√	-			Expired
19.	85/M	CT not done		√	-	-			Expired
20.	56/M	Severe		√	√	-			Expired
21.	61/M	Severe		√	√	-			Expired
22.	57/M	Severe		√	√	-			Expired
23.	71/F	Mild		√	√	-			Expired
24.	55/M	Severe		√	√	-			Survived
25.	53/F	Severe		√	√	-			Expired
26.	60/F	Mild		√	√	-			Expired
27.	80/M	Severe		√	√	-			Expired
28.	66/M	Moderate		√	√	-			Expired
29.	65/M	Severe		√	√	-			Expired
30.	75/M	Severe		√	-	-			Expired
31.	75/M	Mild		√	√	-			Expired
32.	57/M	Severe		√	√	-			Survived
33.	61/F	Mild		√	√	-			Survived
34.	31/M	Severe		√	√	-			Survived
35.	71/M	Mild		√	√	-			Survived
36.	38/M	Severe		√	√	-			Survived
37.	65/F	Severe		√	√	-			Survived
38.	69/F	Severe		√	√	-			Survived
39.	53/M	Severe		√	√	-			Survived
40.	63/M	Severe		√	√	-			Survived
41.	31/F	Severe		√	√	-			Expired
42.	66/M	Severe		√	-	-			Survived
43.	66/M	Moderate		√	-	-			Survived
44.	41/F	Severe		√	-	-			Survived
45.	42/M	Severe		√	√	-			Expired
46.	45/M	Moderate		√	√	-			Survived
47.	39/M	Moderate		√	√	-			Survived
48.	63/M	Severe		√	-	-			Expired
49.	60/F	Moderate		√	-	-			Survived
50.	24/M	Severe		√	√	-			Survived

*__Antifibrotics__ (Pirfenidone) was given to 07 patients who had significant fibrosis & lingering oxygen requirements even after recovery from ventilatory support.
**__IL-6 therapy__ (Tocilizumab) was administered to 05 patients with worsening respiratory parameters despite NIV.

Steroids were given to all the patients with 30 of these patients receiving Dexamethasone (6 mg BD) and 20 patients receiving Methylprednisolone (40 mg BD). Therapeutic low molecular weight heparin (LMWH) was given to 13 patients in view of very high titer of D-Dimer while 37 patients received LMWH as a prophylactic dose. Hence all 50 patients received anticoagulants. All the patients were put on broad spectrum antibiotics ranging from oral doxycycline and azithromycin to the higher intravenous ones due to moderate and severe COVID-19 pneumonia with sepsis.

Amongst the immunomodulators, IL-6 therapy in the form of Tocilizumab was given to five patients who showed worsening parameters even with high NIV supports out of which four patients (80%) survived. Antifibrotic therapy in the form

of oral pirfenidone was given to 07 patients. All therapeutic modalities employed in our patients are depicted in Fig. 6. A summary of Figs. 1–6 is summarized in Table 3.

Discussion

A total of 50 COVID-19 RT-PCR confirmed patients were ventilated over a course of 07 months at our hospital during the first wave of the pandemic. A majority received NIV (N = 39) accounting for 78% of the ventilated patients as against 22% who received IMV (N = 11). There were a total of 25 survivors out of the 50 patients put on mechanical ventilation with 24 in the NIV group and only one in the IMV group. The main reason for putting patients on NIV was a persistent decline in oxygen saturation (SpO2) below 90% despite high flow oxygen via non-rebreathing mask (NRBM) and an increased work of breathing manifesting as tachypnea (respiratory rate $\geq$ 35/min) and use of accessory muscles of respiration. Most of these patients were well oriented and showed reasonable compliance to the NIV (CPAP) mask. Seven patients, however, were converted from NIV to IMV along the course of their illness due to worsening of respiratory parameters including declining SpO2 below 85%, persistently high respiratory rates (usually > 40/min), fatigue and drowsiness despite an increase in NIV supports and clinical and radiological evidence of progressive acute respiratory distress syndrome (ARDS). Most ventilated patients were above the age of 50 years accounting for 74% of the total numbers (N = 37). The 50% mortality rate in all ventilated patients could be attributed to the elderly age group and multiple comorbidities compounding the severity of COVID-19 infection.

CARP was administered to 20 patients while on NIV out of which 14 survived, and 04 patients were administered prone position ventilation while on IMV out of which there was only a sole survivor. CARP could not be given to patients who were too debilitated, were uncomfortable due to body habitus or had a short stay in ICU (mostly under 05 days). CARP did show improved oxygenation in most patients. Prone positioning was attempted in four patients out of the 11 on IMV, mostly the ones with severe ARDS, but only one survived. The other three were more than 55 years in age and had high CT severity.

The main concern raised against the application of NIV in the setting of viral pneumonia is the potential for aerosol dispersion and transmission to health care providers (HCPs). Several studies have reported the use of NIV in severe acute respiratory illness and have demonstrated that it can avoid intubation in up to 70% of patients with mild hypoxic respiratory failure. In a retrospective study on COVID-19 patients, Zhou et al[8] reported that the mortality was higher in the intubated group (96%) than in the NIV group (92%). A similar study on COVID-19 patients by Yang et al[9] revealed a mortality rate of 86% and 57% in the intubated group and the NIV group respectively. Cascella et al showed a favourable outcome of NIV in COVID-19 patients suffering from a non-severe form of respiratory failure along with a low risk of airborne transmission to HCPs with the proper fitting interface.[10] Cheung et al studied the efficacy of NIV and the risk of disease transmission on 20 patients with positive serology for SARS virus treated by NIV and 105 HCPs taking care of these patients. None of 102 HCPs who did the serologic test showed positivity for SARS.[11] In our hospital, though no such transmission to HCPs attending to patients on NIV was studied but stringent adherence to personal protective equipment (PPE) protocols was ensured throughout.

Two phenotypes of Covid-19 lung have been described as namely Type L and Type H. Type L is classically characterized by low elastance, low ventilation to perfusion ratio, low lung recruitability manifesting as a typical interstitial lung edema that may worsen into lung injury (CT scan showing ground glass opacities). These patients typically need high flow nasal oxygen (HFNO) or NIV. Type H patients meanwhile are typically high-elastance, high right-to-left shunt, high lung recruitability and progress into severe ARDS (CT scan showing bilateral infiltrates) which needs classical IMV.[12]

A higher level of pulmonary compliance and shunt fraction is seen in COVID-19 patients with severe ARDS compared to the expected levels of ARDS from other causes.[13] An early study from Wuhan, China, showed a recruitment to inflation ratio (R/I ratio) lower than 0.5 in >80% of COVID-19 patients with severe ARDS, suggesting a significantly poor pulmonary recruitability in COVID-19.[14] Disrupted vasoregulation due to vascular insult has been suggested to be the cornerstone of poor oxygenation in the early stages of ARDS in COVID-19. Thus, pursuing the common treatment approaches of applying high levels of PEEP may accentuate underlying microvascular injury and contribute to a worse outcome.[15] We utilized a low tidal volume and optimal PEEP approach for IMV, the highest PEEP being set at 14 cm H2O, in keeping with the lung protective strategies advocated for ARDS[16] and kept plateau pressures below 30 cm H2O to avoid ventilator induced lung injury (VILI). Despite these measures our mortality with IMV was a staggering 90.9% with only one survivor.

Regarding other therapeutics, as per SOLIDARITY trial, a WHO sponsored project, there was no statistically significant difference in overall 28-day mortality between the patients randomly assigned to Remdesivir treatment and the other group of patients assigned to standard care in patients hospitalized with COVID 19.[17] However there was evidence in favour of usage of Remdesivir in Adaptive Covid-19 Treatment Trial (ACTT-1), which was a randomized, double-blind, placebo-controlled trial, which showed that Remdesivir is an effective treatment for hospitalized adult patients with COVID-19 pneumonia.[18] It resulted in a faster time to recovery, defined as discharge from the hospital or continued

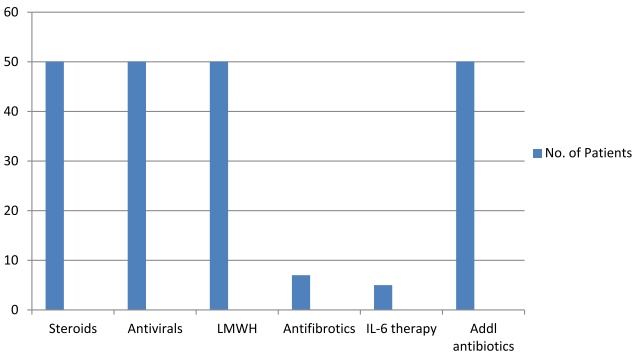


Fig. 6 – Therapeutic modalities employed.

Table 3 – Summary of patient characteristics, ventilatory outcomes and Therapeutic Modalities.

Number of Pateints (Total 50)	**Age Dsiribution (in Years)**						
	21–30	31–40	41–50	51–60	61–70	71–80	81–90
	2	7	5	12	14	8	2
	Gender Distribution						
	Males			Females			
	38			12			
	Prevalent Comorbidities						
	HTN	DM	Obesity	COPD	CKD	CAD	
	14	9	8	6	5	3	
	Types of Ventilation Administered						
	NIV			IMV			
	39			11			
	Final Outcomes of Ventilated Pateints						
	NIV			IMV			
	Survived	Expired		Survived		Expired	
	24	15		1		10	
	Therapeutic Modalities Employed						
	Steroids	Antivirals			LMWH	Addl antibiotics	Antifibrotic	IL-6 Therapy
	50	Ivermectin	Remdesivir	Favipiravir	50	50	7	5
		50	40	8				

hospitalization without need for supplemental oxygen. There was also a statistically significant mortality benefit in patients who were on oxygen supplementation but did not require high-flow oxygen or ventilatory support.

Clinical management protocol for COVID 19 issued by Ministry of Health and Family Welfare (MOHFW), India, gives emergency use authorization to Remdesivir, to be used for patients requiring oxygen supplementation. We administered it to 40 patients requiring mechanical ventilation depending upon the availability of the drug and absence of contraindications. Out of these 20 patients (50%) showed recovery from ventilator and survived the disease. One of our young male patients suffered from COVID-19 induced acute kidney injury (AKI) with creatinine clearance less than 30 ml/min/m^2. This patient was treated with systemic steroids without co-administering Remdesivir and improved with therapy with creatinine normalizing.

Subset of patients suffering from Severe COVID-19 might develop Cytokine Storm Syndrome characterised by markedly raised inflammatory markers namely C-reactive protein (CRP), lactate dehydrogenase (LDH), serum ferritin, D-dimer and pro-inflammatory cytokines (IL-6) along with clinical deterioration.[19] In this regard Tocilizumab is a recombinant humanised anti-IL-6 receptor monoclonal antibody that blocks IL-6 signalling by inhibiting the binding of IL-6 to its receptors and thereby reduces inflammation.[20] Clinical management protocol, issued in 2020 by MOHFW had approved Tocilizumab as off label investigational therapy in patients suffering from moderate COVID-19 disease having progressively increasing oxygen requirements, on mechanical ventilation and not improving despite the use of systemic steroids. There should have been the presence of raised inflammatory markers in these patients. The drug is contraindicated in people living with human immunodeficiency virus (PLHIV), those with active infections (systemic bacterial/fungal), tuberculosis, active hepatitis, absolute neutrophil count < 2000/mm3 and platelet count < 1,00,000/mm^3.[21]

Latest published evidence in support of usage of Injection Tocilizumab came from Randomised Evaluation of COVID-19 Therapy (RECOVERY Trial), an open ended randomised control trial assessing treatment modalities in severe COVID-19 patients admitted in UK. In this trial, patients suffering from hypoxia (oxygen saturation <92% on air or requiring oxygen therapy) and having the evidence of systemic inflammation in form of raised inflammatory marker (CRP ≥75 mg/L) received usual standard of care treatment plus tocilizumab at a dose of 400 mg–800 mg given intravenously.[22]

In our study, we had administered injection tocilizumab at 6 mg/kg body weight to five patients who continued to be hypoxic on NIV support and had raised inflammatory markers in the form of raised IL-6 levels. In cases of delay in availability of IL-6 levels, significantly elevated CRP levels was used as marker of inflammation. Out of these five patients who were on NIV, one progressed to receive invasive mechanical ventilation but was subsequently weaned off successfully. Tocilizumab prevented the progression of cytokine storm in rest of patients. We were able to prevent invasive mechanical ventilation in 3 patients and they were subsequently weaned off NIV. One patient developed invasive fungal infection post tocilizumab therapy requiring IMV. The diagnosis was made based on positive serum galactomann, detection of septate hyphae on broncheolaveolar lavage and CT scan chest findings of multiple nodules with surrounding halo. In view of all this a diagnosis of Invasive Pulmonary Aspergillosis was made. Systemic antifungals were started but the patient succumbed to fungal pneumonia.

Conclusion

We analysed the data of 50 patients of COVID-19 who received mechanical ventilation in our tertiary care hospital in a difficult hilly area (CI zone) over a period of 07 months

during the first wave of the pandemic. With a 50% survival the majority of patients who survived were the ones who received NIV (61.6%). An overwhelming majority of the patients were above 50 years of age (74%) and the mortality was 60% for the ones with comorbidities. These inferences could give us insights about the clinical course expected and the laying down of management protocols of COVID-19 for hospitals in remote areas like ours which could, however, sustain the first wave without depending upon higher medical set ups for help. With subsequent waves of the pandemic expected including the ongoing second one more clinical data needs to be collected to give the medical fraternity a chance to better understand the disease progression, prognosis and ways to manage it.

Disclosure of competing interest

The authors have none to declare.

REFERENCES

1. WHO Main Website. https://www.who.int (accessed April 10, 2021).
2. Jin YH, Cai L, Cheng ZS, et al. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019nCoV) infected pneumonia. *Mil Med Res*. 2020;7(1):4.
3. Huang C, Wang Y, Li X, et al. Clinical features of patients with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020. https://doi.org/10.1016/S0140-6736(20)30183-5.
4. Bhandari S, Singh A, Rankawat G, et al. Characteristics, treatment outcomes and role of hydroxychloroquine among 522 COVID-19 hospitalized patients in jaipur city: an epidemio-clinical study. *J Assoc Phys India*. 2020;68(6):13–19.
5. Ramin R, Reza R, Hashemian SMR. Noninvasive versus invasive ventilation in COVID-19: one size does not fit all!. *Anesth Analg*. 2020. https://doi.org/10.1213/ANE.0000000000004943.
6. Saeed GA, Gaba W, Shah A, et al. Correlation between chest CT severity scores and the clinical parameters of adult patients with COVID-19 pneumonia. *Radiol Res Pract*. 2021;2021:6697677.
7. Weir CB, Jan A. *BMI Classification Percentile and Cut Off Points* [Updated 2020 Jul 10]. In: Stat Pearls [Internet]. Treasure Island (FL): Stat Pearls Publishing; 2021 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK541070.
8. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395:1054–1062.
9. Yang X, Yu Y, Xu J, et al. 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;8:475–481.
10. Cascella M, Rajnik M, Cuomo A, Dulebohn SC, Di Napoli R. *Features, Evaluation and treatment coronavirus (COVID-19)*. Stat Pearls [Internet]. Treasure island (FL): Stat Pearls Publishing; 2020 Jan [Updated 2020 Apr 6]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK554776.
11. Cheung TM, Yam LY, So LK, et al. Effectiveness of noninvasive positive pressure ventilation in the treatment of acute respiratory failure in severe acute respiratory syndrome. *Chest*. 2004;126:845–850.
12. Gattinoni L, Chiumello D, Caironi P, et al. Covid-19 pneumonia: different respiratory treatemnts for different phenotypes. *Intensive Care Med*. 2020. https://doi.org/10.1007/s00134-020-06033-2.
13. Gattinoni L, Coppola S, Cressoni M, Busana M, Chiumello D. Covid-19 does not lead to a "typical" acute respiratory distress syndrome. *Am J Respir Crit Care Med*. 2020;201(10):1299–1300.
14. Pan C, Chen L, Lu C, et al. Lung recruitability in Covid-19-associated acute respiratory distress syndrome: a single-center, observational study. *Am J Respir Crit Care Med*. 2020;201(10):1294–1297.
15. Marini JJ, Gattinoni L. Management of COVID-19 respiratory distress. *J Am Med Assoc*. 2020. https://doi.org/10.1001/jama.2020.6825.
16. The acute respiratory distress syndrome network. *N Engl J Med*. 2000;342(18):1301–1308.
17. WHO Solidarity Trial Consortium, Pan H, Peto R, Karim QA, et al. Repurposed antiviral drugs for covid-19 - interim WHO solidarity trial results. *N Engl J Med*. 2021;384:497.
18. Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for the treatment of covid-19 — final report. *N Engl J Med*. 2020;383:1813–1826.
19. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ, HLH Across Speciality Collaboration, UK. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet*. 2020;395(10229):1033–1034.
20. Zhang X, Peck R. Clinical pharmacology of tocilizumab for the treatment of patients with rheumatoid arthritis. *Expet Rev Clin Pharmacol*. 2011;4(5):539–558.
21. Ministry of Health & Family Welfare. *Guidelines on Clinical Management of COVID-19*. New Delhi: MoHFW, Government of India; 2020. Version 5.
22. Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. *Lancet*. 2021;397:1637–1645.