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Characteristics and Outcomes of COVID-19 Patients Admitted to Adult Intensive Care Unit: A Single-Center Observational Study from the Second Wave in Nepal

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ABSTRACT

Introduction

There is inadequate data of critically ill COVID-19 caused by the delta variant. So, we sought to investigate the characteristics and outcomes during the second wave in Nepal.

Methods

COVID-19 patients admitted to adult ICU of a single institution from April to August 2021 were included. Clinical, laboratory and radiological findings were collected. In-hospital mortality, length of ICU stay, duration of mechanical ventilation (MV) and complications during ICU stay were obtained.

Results

Total 136 patients were included with a mean age of 56.24 (± 15.81) years and 52.2% males. Fifty-five percent had comorbidities. Mean fraction of inspired oxygen required was 0.8 and sequential organ failure assessment score on admission was 4.09. C-reactive protein (CRP), lactate dehydrogenase and ferritin levels were elevated to 62.5mg/L, 515 U/L and 472ng/mL respectively. The computed tomography score was 20. Thirty four (25%) required MV; 70 (52%) were managed with non-invasive ventilation; 41 (30.14%) required vasopressors; 4 (2.9%) required renal replacement therapy. In-hospital mortality was 43.4%. The median length of ICU stay and duration of MV were 6 and 3.5 days respectively. Hospital acquired infection was the commonest complication. Age (OR 1.126 (95% CI 1037-1.223, p value 0.005)) and CRP on admission (OR 1.023 (95% CI 1.000-1.047, p value 0.050) were found to be predictors of mortality.

Conclusion

In this single center study from the second wave of the pandemic, majority of critically ill COVID-19 patients were elderly with co-existing illnesses. In-hospital mortality was high. Age and CRP on admission were found to be independently associated with poor outcome.

Keywords

Characteristics, COVID-19, critical care, Nepal, outcomes

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INTRODUCTION

At the end of 2019, a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that was first identified in China, surged rapidly throughout the world resulting in declaration of a pandemic by World Health Organization on 11 March 2020.[1] The clinical spectrum of the disease, now referred to as Corona virus disease-19 (COVID-19), ranges from mild to critically ill, with reports indicating that 5–9% of cases require intensive care unit (ICU) admission for severe respiratory failure.[2]

Nepal, like most of the neighboring countries, has been hit hard with COVID-19. Especially, the second wave has caused much havoc, with the health system being stretched beyond its capacity, and the government being compelled to execute a whole nation lockdown. Despite the best efforts, an alarming number of lives have been lost and an equal loss of economy has been sustained. ICUs all over Nepal have been the most affected.

Majority of the infections in the second wave of the pandemic that hit Nepal has been reported to be caused by the delta variant of the SARS-Cov-2 virus,[3] which is much deadlier than the other variants. There is inadequate data of characteristic and survival of critically ill Nepalese patients with the delta variant infection, which are important to inform clinical decision making, research and planning for future waves of infection. We therefore conducted a study to evaluate the characteristics and outcomes of critically ill COVID-19 patients in Nepal.

METHODS

This study was a cross sectional observational study conducted during the second wave of the pandemic in critically ill COVID-19 patients admitted to the adult ICU of Nepal Medical College Teaching Hospital (NMCTH), a tertiary care hospital and medical college in Kathmandu, Nepal. Ethical approval was obtained from the Research and Institutional Review Committee, of the same institution. (Ref no.:012-078/079)

General ICU and Neurosurgical ICU of NMCTH were converted to a 16 bedded level III COVID ICU, which was managed as a closed system lead by an intensivist. The inclusion criteria for this study were 1) patients with COVID-19, confirmed with reverse-transcriptase polymerase chain reaction (RT-PCR); 2) 18 years of age and older; and 3) admitted to the adult COVID ICU in line with the WHO guidance on the management of patients with COVID-19[4] and/or the discretion of the treating physician. Patients who were readmitted to the ICU were excluded.

In a recent study done in critically ill COVID-19 patients, the overall mortality was found to be 30.9%.[5] Thus anticipating a similar population proportion (p) of 30.9 % (p=0.309), and using a confidence level of 95% (z = 1.96) and absolute precision of 8 percentage points (d=0.08), the sample size was calculated to be 128.

After obtaining written informed consent from the nearest kin of the patients, the following information were collected: patient demographics, COVID-19 vaccination status, CT severity score at presentation to ICU, day of illness on admission to ICU, oxygen requirement on admission to ICU, SOFA score on admission to ICU, need for respiratory support such as oxygen, noninvasive ventilation and mechanical ventilation, need of vasopressor and renal replacement therapy, abd laboratory parameters (complete blood count, renal function, liver function, inflammatory markers, procalcitonin). Outcomes of the patients in terms of in-hospital mortality, length of ICU stay, duration of mechanical ventilation, and complications occurred during ICU stay were obtained.

Data obtained were entered into Microsoft Excel and IBM® SPSS® Statistics version 16 was used for analysis. Descriptive data were reported as mean ± standard deviation (for normal distribution) or median ± interquartile range (for non-normal distribution) for quantitative variable. Similarly qualitative variables were described in proportions.

A binary logistic regression was also performed to evaluate for predictors of mortality and included demographic factors, clinical features and laboratory parameters on admission to ICU.

RESULTS

The second wave of COVID-19 in Nepal started around mid-April of 2021 and extended up to early August 2021. In these five months, 136 patients that met the inclusion and exclusion criteria were enrolled. The mean age was 56 years (SD 15.81) and 65 (47.8%) of the patients were older than 65 years. The population was equally divided among males and females (52.2% versus 47.8%). Fifty-five percent of the patients had comorbidities. Hypertension (42, 30%) was the commonest co-existing illness followed by diabetes mellitus (30, 22%). Three of the patients with critical pneumonia were pregnant. Patients reported an average 8 days of symptoms before being admitted to the ICU. Most of the patients were admitted from the emergency room (84, 61.8%), and the rest (52, 38.2%) were transferred for clinical deterioration while undergoing treatment in COVID ward or high care unit. (Table 1)

The values of complete blood count, renal function tests, liver function tests and markers of inflammation are listed in Table 1. Hemoglobin levels, total white cell count and platelet counts

Table 1. Characteristics on admission to ICU

Variables	Total number
Age, mean (SD)	56.24 (15.81)
20 to 40 years	22 (16.2)
40 to 60 years	49 (36)
60 to 80 years	54 (39.7)
80 years and above	11 (8.1)
Gender	
Male, n (%)	71 (52.2)
Female, n (%)	65 (47.8)
Comorbidities	
Hypertension, n (%)	42 (30)
Diabetes, n (%)	30 (22)
Respiratory, n (%)	16 (11.7)
Neurological, n (%)	11 (8)
Cardiac, n (%)	4 (2.9)
Renal, n (%)	4 (2.9)
Endocrine, n (%)	6 (4.4)
Malignancy, n (%)	3 (2.2)
Others*, n (%)	3 (2.2)
Obesity, n (%)	5 (3.6)
Day of illness at ICU admission, mean (SD)	8.01 (3.6)
Source of admission	
Emergency, n (%)	84 (61.8)
Ward/ inpatient, n (%)	52 (38.2)
Oxygen requirement on admission to ICU, median (IQR)	0.8 (0.6-1)
SOFA score, mean (SD)	4.09 (1.5)
Vaccination status	
Complete, n (%)	1 (0.007)
Incomplete, n (%)	3 (0.02)
Complete blood count	
Hemoglobin (g/dL), mean (SD)	13.07 (2.03)
Total leukocyte count, median (IQR)	8900 (6125-12950)
Neutrophil lymphocyte ratio, median (IQR)	7.35 (5.19-9.67)
Platelets, median (IQR)	199,000 (152,000- 257,000)
Renal function tests	
Sodium (mmol/L), median (IQR)	137 (135-139)
Potassium (mmol/L), median (IQR)	3.9 (3.7-4.3)
Urea (mg/dL), median (IQR)	26 (16-38)
Creatinine (mg/dL), median (IQR)	0.7 (0.6-0.9)
Liver function tests	
Albumin (g/dL), median (IQR)	3.3 (3-3.6)
Total bilirubin (mg/dL), median (IQR)	0.6 (0.6-0.8)
Direct bilirubin (mg/dL), median (IQR)	0.2 (0.2-0.2)
Aspartate transaminase (IU/L), median (IQR)	42 (24-78)
Alanine transaminase (IU/L), median (IQR)	52 (36-89)
Markers of inflammation and infection	
Ferritin (ng/mL), mean (SD)	472 (322)
Lactate dehydrogenase (U/L) , median (IQR)	515 (335-740)
D- dimer (mg/L), median (IQR)	0.41 (0.34-0.74)
C-reactive protein (mg/L), mean (SD)	62.5 (51.5)
Procalcitonin (ng/ml), median (IQR)	0.38 (0.15-1.24)
CT score, median (IQR)	20 (16-22)

**Others= liver disease (1), psychiatric illness (1), rheumatic disease (1); SOFA: sequential organ failure assessment*

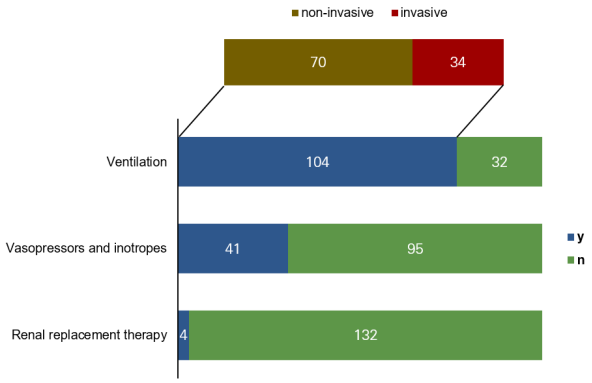

Figure 1. Different types of organ support received

were normal in majority of the patients. Neutrophil lymphocyte ratio (NLR), a marker of severity of COVID-19, was calculated to be 7.35 (5.19-9.67). Renal function tests and liver function tests were within normal range in majority of patients. C-reactive protein was markedly raised to an average 62.5 mg/L. Serum ferritin levels were mildly raised but markedly raised exceeding 1000 ng/mL in 9 patients (6.6%) . Serum lactate dehydrogenase levels were around double the normal values and 11 (8%) had levels above 1000 U/L. D-dimer and serum procalcitonin levels were found to be within normal range. High resolution computed tomography (HRCT) of the chest was performed in 85 of the cases. Ground glass opacities and consolidation were the predominant feature. The average semi quantitative CT severity score was calculated to be 20 (IQR, 16-22).

All patients who required oxygen therapy or higher respiratory support received intravenous corticosteroids. Twelve patients received remdesivir. Tocilizumab was used in one patient and tofacitinib was used in 3 patients.

One hundred and four patients (76.4%) required ventilator support (invasive and non-invasive). Among other organ support, 41 (30.14%) required vasopressors and inotropes for shock and only 4 (2.9%) required renal replacement therapy (Figure 1).

In the study population, 25% of the patients were intubated and underwent invasive mechanical ventilation (IMV). All intubated patients received neuromuscular blockers (over and above that given at the time of intubation) and was placed in prone position at some point during ventilator support. The majority (52%) of the patients was managed using non-invasive ventilation (NIV) only. NIV was provided using single limb portable continuous positive airway pressure or bilevel positive airway pressure (cpap/ bipap) devices with a vented face mask interface and a few using the dual limb system of the ventilator with a non-vented face mask interface. Around 20% received oxygen therapy via various oxygen delivery devices such as

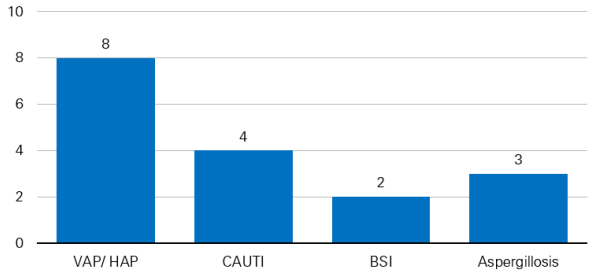

Figure 2. Infectious complications

face mask with reservoir bag, venturi mask, simple face mask and nasal prongs. Remaining 4% did not require any oxygen therapy as they were admitted to the ICU for reasons other than respiratory failure. High flow nasal cannula (HFNC) was used in only one patient, which was used intermittently along with NIV. (Figure 2)

Fifty-nine patients died corresponding to a mortality rate of 43.4%. There were no survivors among those who were intubated and mechanically ventilated. The length of ICU stay was 6 (3-12) days. The duration of mechanical ventilation was 3.5 (2-7) days.

There were 17 incidences of infectious complications. The commonest hospital acquired infection was bacterial pneumonia, which included one hospital acquired pneumonia (HAP) and 7 ventilator associated pneumonia (VAP). The VAP rate was calculated to be 39 per 1000 ventilator days. Other infections include 4 catheter associated urinary tract infections, 2 blood stream infections, and 3 invasive aspergillosis. There were no cases of mucormycosis (Figure 2).

There were 39 events of other major complications. Among them delirium was the commonest (11) followed by acute kidney injury (8) and type 2 respiratory failure (6). Four patients also had pneumothorax, among which 2 were tension pneumothorax directly leading to mortality. The details of all the major complications recorded are given in Figure 3.

A binary logistic regression evaluated for predictors of in-hospital mortality (Table 2). Among the many variables, age was found to be the most reliable predictor of mortality, with an OR of 1.126 (95% CI 1037-1.223, p value 0.005). CRP level was also the other indicator that predicted mortality with an OR of 1.023 (95% CI 1.000-1.047, p value 0.050). Other factors were not found to be significantly associated with mortality.

DISCUSSION

In this single center observational study, characteristics and outcome of 136 critically ill COVID-19 patients during the second wave in Nepal were evaluated.

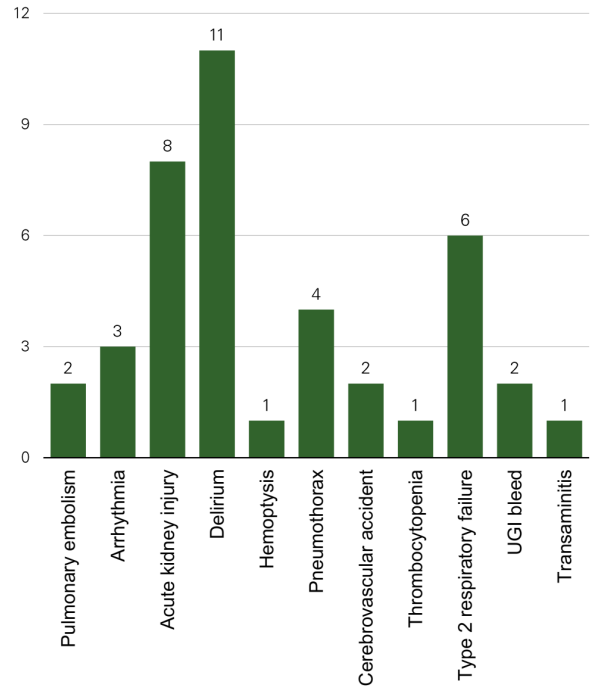

Figure 3. Other major complications

Around half of the population in this cohort was elderly with co-existing illness, mainly hypertension and diabetes mellitus. This finding concurs with other data, which also suggest elderly population and comorbid conditions are associated with critical illness in COVID-19.[6-9] However, obesity was not a common finding, unlike in other studies, where as high as half the patients were obese.[10] This may be due to the reason that obesity is not common in the general population of Nepal as in the Western society. In contrast to other studies, where there was male predominance,[6-9,11] there was no gender predisposition in the patients admitted to our ICU.

Laboratory parameters were mostly within normal limits except the neutrophil lymphocyte ratio (NLR), which has been shown to be a marker of severity of illness in COVID-19. The NLR was found to be 7.35. An NLR of >4 was a predictor of ICU admission in a study by Cicullo et al.[12] Inflammatory markers, which have been shown to be reliable prognostic markers, were shown to be raised at the time of admission, especially CRP. However, D-dimer was mostly normal, in contrast to other studies, where the values were raised up to 1- 2U/L.[13,14] Serum procalcitonin, like in other studies,[14,15] was within normal range. This indicates that most patients admitted to ICU arrived with a progression of the disease process itself rather than due to secondary bacterial infection.

The patients admitted to our ICU had severe hypoxemic respiratory failure as suggested by the high oxygen requirements (average FIO_2 required of 0.8, and maximum patients required high flow oxygen therapy of 15L/min or more approximating an FIO2 of 1), and a high CT severity score (an average of 20). Around 50% of the patients had to upgrade the respiratory support to NIV and 25% required IMV. This also indicates that majority of the patients admitted to our ICU were very critical. Furthermore, the proportion of invasive ventilation underestimates the severity as many patients, a lot owing to the age factor, opted for do-not-intubate directives. There seems to be variation in the rates of IMV worldwide, with US and Italy having a higher rate of 60-88% and lesser in China ranging from 15-42%.[4-5,8-9, 16-17] This variability may be explained by the differences in population characteristics, as well as the provision of care, including the use of NIV strategies. High flow nasal cannula was rarely used as most patients were much more critical, requiring higher positive end expiratory pressure (PEEP), and adequate oxygenation could not be achieved with

Table 2. Binary logistic regression

Factors	Odds ratio	95% confidence interval		p-value
		Lower	Upper	
Age	1.126	1.037	1.223	0.005
Presence of comorbidity	0.805	0.132	4.890	0.81
Male gender	1.783	0.321	9.909	0.51
Oxygen requirement on admission	1.029	0.991	1.069	0.06
Total count	1.000	1.000	1.000	0.85
Neutrophil lymphocyte ratio	0.985	0.846	1.147	0.85
Platelets	1.000	1.000	1.000	0.67
Creatinine	22.79	0.396	1311.835	0.13
Albumin	6.534	0.767	55.660	0.09
Ferritin	0.999	0.997	1.002	0.57
Lactate dehydrogenase	1.000	0.996	1.003	0.84
D-dimer	0.414	0.066	2.598	0.35
C-reactive protein	1.023	1.000	1.047	0.05
Procalcitonin	1.016	0.838	1.232	0.87
SOFA score	1.258	0.684	2.313	0.46

it. Overwhelmed with the surge of patients, the severe shortage of oxygen supply in the hospital (as well as all over the city) unable to match the oxygen consumption demanded by HFNC also restricted its use during the pandemic. The severity of illness of the patients was also assessed using SOFA score. A SOFA score of 4 was obtained, which was comparable to studies by Xie et al. and Narsullah et al.[15,18]

Treatment of COVID-19 varied with time as numerous studies were published during the study period. The RECOVERY trial[19] was already published prior to this study, so all patients who had supplemental oxygen were administered intravenous corticosteroids, but the dosing and type varied as more studies explored for better results. Remdesivir was used in only a few of the patients, and only in those who presented within 10 days of illness and were not ventilated. The REMAP-CAP trial of tocilizumab had also been published recently showing positive outcome.[20] However, limited availability and very high cost of the drug hindered the use of the IL-6 inhibitor. We used tofacitinib in a few patients, after another trial showing some benefit.[21] The use of vasopressors was in a third of the patients, which is slightly less than other studies, where 40-60 % of patients requiring such therapy have been reported.[10] Renal replacement therapy was required in only 3% of the patients, in contrast to other studies where its use is much higher.[10]

The overall in-hospital mortality in the present study was 43.4%, which is considerably high but comparable to other studies, where rates have varied from 14-67%.[5-6,8-9,16-17,22-23] The absence of vaccination against COVID-19 in majority of our patients may have resulted in lower chances of survival. During the study period, national vaccination program against COVID-19 was in an early phase so general population was yet to receive the vaccines.

No patients who required invasive ventilation survived. Survival of intubated patients in COVID-19 has been very bleak all around the world with a reported mortality rate of 85-97% in other studies[11,24] These data are also derived from studies when the delta variant was not prevailing. We opted for delayed initiation of invasive ventilation, which could have resulted in the sickest patients receiving IMV, resulting in survival chances in this cohort being extremely low.

The commonest infectious complication was VAP with a rate of 39 per 1000 ventilator days. Though this is quite high, it is comparable to studies which also suggest that VAP rates may be higher in COVID patients than non-COVID patients.[25] Among the non-infectious complications, delirium was the commonest major complication reported followed by acute kidney injury. A wide range of complications attributed to COVID-19 were found, including cerebrovascular accidents, and pneumothorax, with 2 patients succumbing to tension pneumothorax. The incidence of pulmonary embolism was not common with only two cases being detected. This is in stark contrast to other studies, where the incidence of PE has been reported to be 16.5%.[26] The difference can be attributed to the lower use of CT pulmonary angiography to investigate for PE.

The binary logistic regression found advanced age and high CRP values on admission to ICU to be the only variables predictive of mortality. This is in agreement to many studies that have consistently reported age to be independently associated with mortality.[10,15,18] A study form Nepal by Sharma S et al. also found CRP values on admission to be a predictor of mortality.[11]

There are various limitations of this study. The end points of the study were limited to hospital stay, therefore, we cannot conclude regarding long term outcomes. Being a single center cross sectional study, the results cannot be generalized to other centers, countries or races. The study only documented clinical, radiological and laboratory findings at the time of presentation to ICU. Many other factors during the course of stay, and a multitude of parameters, including therapy details, and resource allocation could influence patient outcome. However, as this is a descriptive study, even inclusion of all clinical details will not be hypothesis generating. Furthermore, considering the study was done in the period when the whole nation was in a crisis, it must be pointed out that the scarcity of beds, drugs and even oxygen could have influenced the outcome.

CONCLUSION

This observational study provides characteristics and outcomes of COVID-19 patients admitted during the second wave in a single center adult ICU in Nepal. Majority of patients were elderly, had co-existing illnesses and were admitted for severe hypoxemic respiratory failure. NIV was the commonest respiratory support used but IMV and vasopressors were also frequently required. Overall in-hospital mortality was high, and survival chances even lower in those requiring IMV. VAP was the commonest infectious complications and delirium often complicated the ICU stay. Age and CRP on admission were two factors found to be independently associated with poor outcome.

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CONFLICT OF INTEREST

The author(s) declare that they do not have any conflicts of interest with respect to the research, authorship, and/or publication of this article.

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REFERENCES

1. Waris A, Atta U, Ali M, et al. COVID-19 outbreak: current scenario of Pakistan. New Microbes New Infect 2020; 35: 100681.
2. Lenka J, Chhabria MS, Sharma N, et al. Clinical characteristics and outcomes of critically ill patients with COVID-19 in a tertiary community hospital in upstate New York. J Community Hosp Intern Med Perspect. 2020 Oct 29;10(6):491-500.
3. Nepali Times. Delta variant's wake-up call for Nepal [Internet]. Kathmandu: Nepali Times; 2021. [updated 2021; cited 2021 Oct 27]. Available from: https://www.nepalitimes.com/here-now/delta-variants-wake-up-call-for-nepal.
4. World Health Organisation. Clinical management of COVID-19. 2020 May 27; Available from: https://www.who.int/publications/i/item/clinical-management-of-covid-19
5. Auld SC, Caridi-Scheible M, Blum JM, et al. and the Emory COVID-19 Quality and Clinical Research Collaborative. ICU and Ventilator Mortality Among Critically Ill Adults With Coronavirus Disease 2019. Crit Care Med. 2020 Sep;48(9):e799-e804.
6. Grasselli G, Zangrillo A, Zanella A, et al; COVID-19 Lombardy ICU Network. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. JAMA. 2020 Apr 28;323(16):1574-1581.
7. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA. 2020 Mar 17;323(11):1061-1069.
8. Bhatraju PK, Ghassemieh BJ, Nichols M, et al. Covid-19 in Critically Ill Patients in the Seattle Region - Case Series. N Engl J Med. 2020 May 21;382(21):2012-2022.
9. Cummings MJ, Baldwin MR, Abrams D, et al. Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study. Lancet. 2020 Jun 6;395(10239):1763-1770.
10. Thomson RJ, Hunter J, Dutton J, et al. Clinical characteristics and outcomes of critically ill patients with COVID-19 admitted to an intensive care unit in London: A prospective observational cohort study. PLoS One. 2020 Dec 15;15(12):e0243710.
11. Sharma S, Paneru HR, Shrestha GS, et al. Characteristics and Outcome of Patients with COVID-19 Undergoing Invasive Mechanical Ventilation for Respiratory Failure in a Tertiary Level Hospital in Nepal. J Nepal Health Res Counc. 2021 Sep 6;19(2):396-401.
12. Ciccullo A, Borghetti A, Zileri Dal Verme L, et al; GEMELLI AGAINST COVID Group. Neutrophil-to-lymphocyte ratio and clinical outcome in COVID-19: a report from the Italian front line. Int J Antimicrob Agents. 2020 Aug;56(2):106017.
13. Banno A, Hifumi T, Okamoto H, et al. Clinical characteristics and outcomes of critically ill COVID-19 patients in Tokyo: a single-center observational study from the first wave. BMC Infect Dis. 2021 Feb 9;21(1):163.
14. Guo F, Xie J, Wu W, et al. Clinical characteristics and outcomes of critically ill patients with coronavirus disease 2019 with hypotension in China: a retrospective cohort study. Ann Palliat Med. 2021 Aug;10(8):8536-8546.
15. Nasrullah A, Jayakrishnan T, Wedgeworth P, et al. Characteristics and Outcomes of COVID-19 Patients Admitted to Intensive Care Units in a Large Health System in Western Pennsylvania. Cureus. 2021 Jul 22;13(7):e16552.
16. Arentz M, Yim E, Klaff L, et al. Characteristics and Outcomes of 21 Critically Ill Patients With COVID-19 in Washington State. JAMA. 2020 Apr 28;323(16):1612-1614.
17. Ferguson J, Rosser JI, Quintero O, et al. Characteristics and Outcomes of Coronavirus Disease Patients under Nonsurge Conditions, Northern California, USA, March-April 2020. Emerg Infect Dis. 2020 Aug;26(8):1679-1685.
18. Xie J, Wu W, Li S, et al. Clinical characteristics and outcomes of critically ill patients with novel coronavirus infectious disease (COVID-19) in China: a retrospective multicenter study. Intensive Care Med. 2020 Oct;46(10):1863-1872.
19. RECOVERY Collaborative Group, Horby P, Lim WS, Emberson JR, et al. Dexamethasone in Hospitalized Patients with Covid-19. N Engl J Med. 2021 Feb 25;384(8):693-704.
20. REMAP-CAP Investigators, Gordon AC, Mouncey PR, Al-Beidh F, et al. Interleukin-6 Receptor Antagonists in Critically Ill Patients with Covid-19. N Engl J Med. 2021 Apr 22;384(16):1491-1502.
21. Guimarães PO, Quirk D, Furtado RH, et al; STOP-COVID Trial Investigators. Tofacitinib in Patients Hospitalized with Covid-19 Pneumonia. N Engl J Med. 2021 Jul 29;385(5):406-415.
22. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020 Feb 15;395(10223):497-506.
23. Wang Y, Lu X, Li Y, et al. Clinical Course and Outcomes of 344 Intensive Care Patients with COVID-19. Am J Respir Crit Care Med. 2020 Jun 1;201(11):1430-1434.
24. 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 Mar 28;395(10229):1054-1062.
25. Maes M, Higginson E, Pereira-Dias J, et al. Ventilator-associated pneumonia in critically ill patients with COVID-19. Crit Care. 2021 Jan 11;25(1):25.
26. Suh YJ, Hong H, Ohana M, et al. Pulmonary Embolism and Deep Vein Thrombosis in COVID-19: A Systematic Review and Meta-Analysis. Radiology. 2021 Feb;298(2):E70-E80.