Original Article

Mortality Rate of COVID-19 Patients in Intensive Care Unit: A Multicentre Retrospective Observational Study

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ABSTRACT

The case of Coronavirus Disease 2019 (COVID-19) is growing rapidly worldwide. More than 6 million people in Indonesia were confirmed to be infected as of March 2022. This disease caused an increase in the demand of respiratory assistance and intensive care services back in 2021. Unfortunately, the report about COVID-19 case in Intensive Care Unit (ICU) of Indonesia is very scarce although it is very crucial to evaluate the treatment approach and the prognosis of the patients. This study aimed to determine the characteristics, therapy, and outcomes of critically ill COVID-19 patients treated in the ICU. This was a multicentre retrospective study conducted in 12 hospitals in Indonesia from April 2020 to March 2021. All data regarding the characteristics, therapy, and outcomes of COVID-19 patients admitted to ICU were recorded and analysed. 1,502 patients were included in this study. Inpatient mortality occurred in 44.67% patients. The highest morbidity is attributed to stroke (83.4%). We found a significantly longer duration of mechanical ventilation use in non-survivors group (5.57 vs. 1.74 hours). Furthermore, the results of this study showed a significant difference in all type of treatment (excluding antifungal) between two groups. The mortality of COVID-19 patients in ICU is considerably high. Hypothyroidism and DMII patients showed a high serum asprosin, which linked with poor glycemic and lipid management. It is a biomarker for diabetes and thyroid issues.

GRAPHICAL ABSTRACT
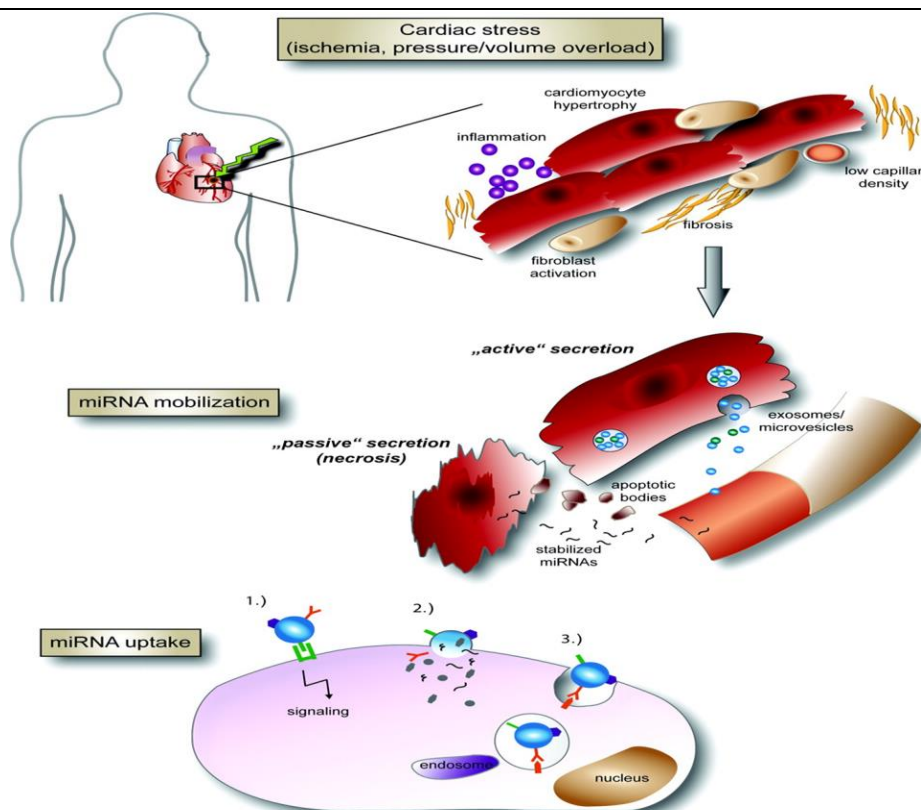
Introduction

Since December 2019, Coronavirus Disease 2019 (COVID-19) has infected more than 400 million people worldwide and caused over 6 million deaths. In Indonesia, 6,338,906 cases people were confirmed to have the disease and 157,478 of them died as of August 2022 [1]. COVID-19 has a broad clinical spectrum, from the mild to critical cases requiring intensive care [2]. The SARS-COV2 virus spreads rapidly so that the number of patients requiring respiratory assistance is also increasing. This condition causes an increase in demand for intensive care unit (ICU) services, which from the latest data demonstrates a high mortality rate for critical COVID-19 patients [3-5].

Preliminary data from a single centre in Wuhan indicate a significant mortality rate with 61.5% of patients dying within 28 days of ICU stay [6]. Since then, multicentre studies have begun to develop, and a national study in Sweden showed a lower mortality rate, 26.7% within 30 days [7]. However, data from the United States show a high ICU mortality, especially in mechanically ventilated patients who are still above 30%. The same conditions were also found in other centres with adequate facilities [8]. Meanwhile, in Indonesia, the number of COVID-19 studies is still limited and until now there has been no research in the ICU.

Several studies have tried to describe the characteristics and comorbidities in patients with SARS-CoV infection [9, 10]. However, there are no publications that discuss COVID-19 patients in the ICU specifically including their characteristics, therapy, and outcomes. This population data is very crucial in determining the prognosis and evaluating the treatment approach that has been implemented so far. This study aimed to determine the characteristics, therapy, and outcomes of critically ill COVID-19 patients treated in the ICU.

Materials and Methods

This is a retrospective multicentre study by using medical record instruments carried out in the COVID-19 ICU starting from the beginning of one-year treatment from April 2020 to March 2021. The target population is COVID-19 critical adult patients at twelve hospitals (Adam Malik Hospital Medan, Dr. M. Hoesin Hospital Palembang,

Wahidin Sudirohusodo Hospital Makassar, Universitas Hasanuddin Hospital, Moewardi Hospital Solo, Mattaher Hospital Jambi, Sanglah Hospital Denpasar, Kariadi Hospital Semarang, Awal Bros Hospital Batam, Universitas Indonesia Hospital Jakarta, Dr. Cipto Mangunkusumo Hospital, and Hasan Sadikin Hospital Bandung). Inclusion criteria were patients aged >18 years with COVID-19 diagnosis and admitted to ICU. Patients with incomplete medical record data were excluded from the study.

Subjects were taken by total sampling method. All collected data will be uploaded to a website called Research Electronic Data Capture (REDCap). REDCap allows collaborators in those 12 hospitals to input and store data on a secure system. The research team from the hospital will be given the REDCap server login details to enter the data securely into the system. The patient's name will be concealed in the report. The username and password given by the coordinator of the research organizer will not be disseminated and only certain people appointed by the main researcher can access the REDCap server. The REDCap server is managed by the Universitas Indonesia. This study has been approved by the Ethics Committee with the reference letter number of 841/UN4.6.4.5.31/PP36/2020.

The statistical analysis was performed by using Stata version 15 (College Station, Texas 77845 USA). Counts and percentages were used to summarize categorical variables. Continuous variables were summarized by using mean ± standard deviation (SD) or median. Chi-square tests were used to assess the association between categorical clinical or laboratory parameters and study outcomes. Independent t-test were used to determine the association of continuous variables, with the study outcomes. Hypothesis testing was performed at 5% level of significance.

Results and Discussion

1502 patients were included in this study. Table 1 represents the baseline characteristics and outcomes of study population. We found that the mortality rate of our subject is 44.67% (Figure 1).
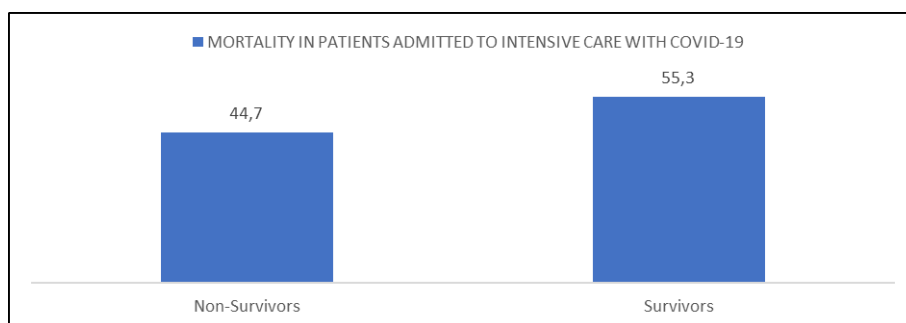

Figure 1: Mortality in patients admitted to intensive care with COVID-19

Table 1: Baseline characteristics and outcome of study population

Variables	All (n=1502)	Non-Survivors (n = 671)	Survivors (n = 831)	Sig.
Age (mean±SD)	47.77±12.88	48.03±12.91	46.88±12.96	0.1849
BMI (mean±SD)	24.27±3.48	24.14±3.41	24.46±3.60	0.1445
Length of stay in ICU (days)	5.98±6.19	6.19±5.53	6.08±6.69	0.7322
Duration of Mechanical Ventilation (days)	1.86±3.91	3.33±4.68	0.77±2.78	0.0000

Table 2 lists that respiratory parameters, neurological parameters, hematological parameters, hemodynamic parameters, and liver and metabolic parameters that did not differ significantly. The therapeutic protocol applied to COVID-19 patients in ICU revealed good results, although the mortality rate was quite high.

Based on the results of our study, we found that the mortality rate of our study population is considered high as 44.67%. The high mortality of

patients admitted to ICU indicates the presence of severe complications [11]. According to data reported in the United States, the mortality of COVID-19 patients in the ICU is estimated at 67% in Washington and 32% in the United Kingdom [9].

Table 2: Multiple parameters of study population

Respiratory Parameters (mean±SD)	All (n=1502)	Non-Survivors (n=671)	Survivors (n=831)	Sig.
Respiratory rate /min	25.63±5.64	26.19 ± 6.11	25.10 ± 5.18	0.0015
SpO2 %	93.21±7.17	91.77 ± 7.85	95.05 ± 5.75	<0.001
pH	7.41±0.13	7.38 ± 0.13	7.44 ± 0.13	<0.001
$PaCO_2$	38.07±15.01	39.10±15.85	37.03 ± 13.01	0.0166
PaO_2	100.95±43.47	95.60 ± 43.56	104.87 ± 42.93	0.0003
HCO_3	22.96±6.42	22.37 ± 6.34	23.65 ± 6.46	0.0029
BE	-0.23±8.14	-1.91 ± 7.85	1.52 ± 8.03	<0.001
PF Ratio	137.91±107.27	122.69 ± 92.49	160.55 ± 122.80	<0.001
Neurological Parameters (mean±SD)				
Glasglow Coma Scale (GCS)	14.21±1.94	13.90 ± 2.31	14.47 ± 1.49	<0.001
Hematological Parameters (mean±SD)				
Hemoglobin g/dL	12.52±2.68	12.59 ± 2.57	12.46 ± 2.76	0.3885
Hematocrit %	37.79±8.20	38.11 ± 8.28	37.49 ± 8.13	0.1984
Neutrophil %	81.29±12.72	83.82±11.9	79.49 ± 12.98	<0.001
Lymphocytes %	10.37±7.32	8.66 ± 6.16	11.58 ± 7.81	<0.001
Neutrophil Lymphocytes Ratio (NLR)	14.65±14.78	17.55±16.64	12.59±12.92	<0.001
International Normalized Ratio (INR)	1.13±0.21	1.15 ± 0.233	1.11 ± 0.18	0.0233
Fibrinogen mg/dL	476.26±200.89	483.41 ± 214.92	466.73 ± 180.83	0.4616
D-Dimer mg/L	5.31±7.88	5.48 ± 7.37	5.18 ± 8.26	0.5612
Hemodynamic Parameters (mean±SD)				
Systolic mmHg	127.29±23.13	127.21 ± 24.54	127.39 ± 11.17	0.9057
Diastolic mmHg	75.81±13.48	75.75 ± 14.78	75.88 ± 11.51	0.8811
Mean Arterial Pressure (MAP) mmHg	93.53±16.52	93.88 ± 17.73	93.17 ± 15.16	0.4889
Body Temperature °C	36.96±0.75	37.02 ± 0.84	36.91 ± 0.66	0.0131
Liver and Metabolic Parameters				
Total Bilirubin mg/dL	1.22±1.68	1.30 ± 1.71	1.13 ± 1.66	0.302
Direct Bilirubin mg/dL	0.69±1.24	0.70 ± 1.18	0.69 ± 1.30	0.9216
Indirect Bilirubin mg/dL	0.43±0.35	0.41 ± 0.30	0.45 ± 0.39	0.2901
SGOT U/L	90.35±182.28	100.14 ± 185.46	82.85 ± 179.6	0.116
SGPT U/L	73.34±164.02	80.38 ± 179.34	67.89 ± 151.02	0.1986
Albumin g/dL	3.05±0.6	2.92 ± 0.63	3.14 ± 0.56	<0.001
Renal Parameters				
Ureum mg/dL	57.38±58.1	61.43 ± 60.8	53.38 ± 55.08	0.0243
Creatinine mg/dL	2.15±0.94	2.36± 3.28	1.94 ± 3.05	0.0248
Electrolyte Parameter				
Sodium mmol/L	135.13±6.4	134.71 ± 6.81	135.44 ± 6.07	0.0454
Potassium mmol/L	4.05±0.88	4.11 ± 0.93	4.01 ± 0.84	0.0556
Chloride mmol/L	103.87±7.55	104.73± 8.15	103.21 ± 7.37	<0.001

This rate is consistent with findings across the globe by Armstrong *et al.*, showing an overall of 41.6%, ranging from 34.0% to 49.7%, obtained from the data of 24 studies which included 10,150 patients from several countries and centres [4]. Compared with some early reports of COVID-19 from Wuhan, with mortality rates of ICU patients ranging from 52 to 62% and

increased to 86–97% among those requiring invasive mechanical ventilation, it is clear that the mortality rate of COVID-19 patients in the ICU is declining. Reports by Intensive Care National Audit & Research Centre (ICNARC) also indicating a peak at 52% in April 2020, and downtrend in mortality in the following months. The update of study by Armstrong *et al.* also show a decreasing mortality rate with an overall of 35.5% [12, 13].

The downtrend of mortality rate of COVID-19 patients in ICU is found uniformly across the globe despite differences in demographic characteristics, comorbidities, ICU admission criteria, treatments, and interventions done to the patients. It is believed that the increase of healthcare experiences and studies related to the diagnosis and treatment of COVID-19 has made this trend possible. Furthermore, a decline in the viral load is suggested to play a role in the declining mortality rate of COVID-19. This is shown in a study conducted in Michigan, comparing the viral load of hospitalized COVID-19 patients during the period of April 2020-June 2020, which notice a reduction of the "high viral load category" from a 25.5% to a zero percent in the sixth week of study. Thus, making the viral load being use to assess the severity of the pandemic [3].

This is the first multicentre retrospective observational study of outcomes of patients admitted to ICU with COVID-19 in Indonesia. Even though, the first COVID-19 was reported in Indonesia on March 2, 2020 with two cases. Data on March 31, 2020 showed that there were 1,528 confirmed cases and 136 deaths. The COVID-19 mortality rate in Indonesia is 8,9%, this figure is highest in Southeast Asia. As of March 30, 2020, there were 693,224 cases and 33,106 deaths worldwide. Europe and North America have become the epicentre of the COVID-19 pandemic, with cases and deaths already surpassing China. The United States ranks first with the most COVID-19 cases with the addition of 19,332 new cases on March 30, 2020, followed by Spain with 6,549 new cases. Italy has the highest mortality rate in the world, at 11.3% [14]. This number of case reports confirms the human-to-human transmission of coronavirus infection pneumonia. Currently, there is no effective therapy or vaccine for coronavirus infection pneumonia. This study tries to report the outcome of Covid-19 patients who received therapy according to the WHO protocol.

Conclusion

The mortality of COVID-19 patients in ICU is considerably high. The high mortality of patients admitted to ICU indicates the presence of severe complications.

Acknowledgments

Authors' contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

Conflict of Interest

There are no conflicts of interest in this study.

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