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ORIGINAL RESEARCH **INTENSIVE CARE**

SAPS 3 as a 28-day mortality predictor in critically ill COVID-19 patients

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Abstract

Background: The case fatality rate (CFR) of COVID-19 was 8.7% in Indonesia on April 2020. Simplified Acute Physiology Score 3 (SAPS 3) has been used to predict the hospital mortality based on different variables including acute physiologic derangements, current conditions and interventions, and previous health status assess the severity of condition during the first hour of admission to the ICU. We assessed SAPS 3 to predict the outcome and mortality of critical COVID-19 patients in ICU over a period of 28 days.

Methodology: This retrospective cohort study consisted of adult patients admitted to ICU with probable or confirmed COVID-19 in our hospital. We recorded the patients SAPS 3 score from the medical record as well as the 28-day mortality. Validity of the SAPS 3 score was done by the Area Under Curve (AUC) measurement and Hosmer-Lemeshow calibration test.

Results: The mortality rate of critical COVID-19 patients was 43.8%. The age, intra-hospital location before ICU admission, use of vasoactive drugs ($P < 0.0001$), focal neurological deficits ($P < 0.0001$), respiratory failure ($P = 0.004$), creatinine ≥ 3.5 mg/dL ($P = 0.005$), and platelets < 50,000 /µL ($P = 0.032$) were significantly associated with 28-days mortality in the ICU. SAPS 3 showed good discrimination and predictability. The optimal cut-off point was 39 with 70.3% sensitivity and 74.4% specificity.

Conclusion: SAPS3 score system was valid in predicting the 28-day mortality of COVID-19 patients in the ICU with good discrimination and calibration value; therefore, it is an important predictor tool for early prognosis screening that will help reduce the strain over the ICU resources.

Abbreviations: CFR: Case Fatality Rate; SAPS 3: Simplified Acute Physiology Score 3; COVID-19: The Coronavirus Disease 2019; ICU: Intensive Care Unit; APACHE: Acute Physiology and Chronic Health Evaluation; SPSS: Statistical Package for Social Sciences; GCS: Glasgow Coma Scale; ROC*: Receiver Operating Characteristic;* PHEIC: Public Health Emergency of International Concern; OR: Odds Ratio;

Key words: COVID-19; Hospital Mortality; Humans; Intensive Care Units; Prognosis; Respiratory Insufficiency; ROC Curve; SARS-CoV-2; Severity of Illness Index; Simplified Acute Physiology Score 3

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1. Introduction

The Coronavirus Disease (COVID-19) outbreak has become a worldwide health problem. On December 31, 2019, the China Country Office, WHO, reported a pneumonia case of unknown etiology in Wuhan City, Hubei Province, China. This was identified later as a new type of coronavirus infection (coronavirus disease, COVID-9) called SARS-CoV-2.[1] Almost a month later the situation escalated globally as WHO declared it as a Public Health Emergency of International Concern (KKMMD/PHEIC), as the cases increased and spread rapidly across the countries.[2]

Patients with severe symptoms of COVID-19 needed to be kept in the intensive care units (ICU). Prioritizing the limited ICU beds and resources to treat large number of patients has been troublesome, since there are no current prognostic biomarkers to determine the severity and mortality of COVID-19 in the ICU.

The SAPS 3 model predicted hospital mortality of adults requiring tertiary- level care in ICU with good calibration and fair discrimination.[3] It can predict mortality more accurately, and with higher sensitivity compared to Acute Physiology and Chronic Health Evaluation-II (APACHE- II) scoring system.[4] SAPS 3 can reduce the strain on ICUs with a high bed occupancy rate in Indonesia. The objective of this study to validate and assess SAPS 3 scoring system as a predictor of 28-day mortality, specifically for COVID-19 patients in an ICU.

2. Methodology

This retrospective cohort study was conducted in ICUs of Cipto Mangunkusumo Hospital and Universitas Indonesia Hospital, between March-August 2020. There were 312 inpatient and 1069 outpatient patients treated at these hospitals with probable and/or confirmed COVID-19 during the study period. The study protocol was approved by the Ethics Committee of the Faculty of Medicine, Universitas Indonesia number KET-746/ UN2.F1/ETIK/PPM.00.02/2020. By using the rule of thumb formula, 200 patients were recruited as samples.

Secondary data from medical records and ICU registries were extracted by the research assistant team. Researchers recorded the patient's basic characteristics such as gender and length of stay in the ICU. They also recorded data that was needed to assess the SAPS 3 score from patients' medical records, such as age, comorbidity, use of vasoactive drugs before ICU admission, intra-hospital location before ICU admission, length of hospital stay before ICU admission, reasons for ICU admission, surgical status at ICU admission, and any acute infection at ICU admission.

The patient's physiological status was recorded in the first hour of admission to ICU including the lowest Glasgow Coma Scale (GCS), the highest readings of heart rate, systolic blood pressure, bilirubin level, body temperature, creatinine level, and the leucocytes count; and the lowest platelets count and the pH, the use of ventilators and oxygenation, and the outcome of the patient on the 28th day after admission to ICU. The patients, who returned home before 28 days hospitalization were followed up by telephone.

Suspected COVID-19 case was defined as;

a. A patient with acute respiratory infection (presence of fever with cough or difficulty of breathing) and history of travel to places with high prevalence of COVID-19 within 14 days;

b. A patient with acute respiratory infection, and one who had direct contact with COVID-19 within 14 days; and

c. A patient with severe acute respiratory illness (presence of fever with cough or difficulty of breathing that needed hospital care, with no alternative diagnosis to explain the symptoms). *Probable COVID-19 case* was defined as a patient with suspected COVID-19 diagnosis with unspecific laboratory results.

Confirmed COVID-19 case was defined as a patient with positive results from laboratory examination.[12]

Inclusion criteria were adults (≥ 18 y old), probable and confirmed COVID-19 patients in ICU care (in Cipto Mangunkusumo Hospital and Universitas Indonesia Hospital) between March-August 2020. We excluded patients with incomplete medical records and probable and confirmed COVID-19 patients with unknown status of life before ICU admission.

All collected data were analyzed using Statistical Package for Social Sciences (SPSS) version 25. Bivariate analysis was conducted to determine the correlation between the SAPS 3 variable and the 28-day mortality variable. If the independent variable was categorical, the bivariate analysis used was the Chi-Square or Fisher's Exact test. If the independent variable was numerical, then the analysis of the bivariate used was T-unpaired or Mann-Whitney test. Multivariate logistic regression was conducted to determine the SAPS 3 significance in predicting 28-day mortality. The variables included in the logistic regression analysis were those that had a $P < 0.25$ in the bivariate analysis.

An external validation test was conducted on the SAPS 3 based on the discrimination value and the calibration value. Calibration values were performed using the Hosmer-Lemeshow test. The optimal cut-off value was

determined based on the highest Youden index based on data from the *Receiver Operating Characteristic* (ROC) curve. Sensitivity and specificity, then were calculated. The comparison between mortality and categorization of the SAPS 3 based on the cut-off point was analyzed using the Chi-square test/Fisher exact test.

3. Results

During the sampling period, there were 213 patients admitted to the ICU with probable and confirmed COVID-19. Five patients were excluded due to missing medical records or incomplete data. In total 208 subjects were analyzed. The patients' characteristics are presented in Table 1. From all of the recruited subjects, 45.6% of the subjects were confirmed COVID-19 patients and the 28-day mortality rate was 42.1%.

Table 1: Characteristics of research subjects

Variable	N (%) (n = 208)	Average / Median
Gender		
▪ Men	144 (69.2)	
▪ Women	64 (30.7)	
Age *		50.6 ± 16.3)
COVID-19 Status		
▪ Probable	113 (54.4)	
▪ Confirmed	95 (45.6)	
ICU length of stay **		9 (1-57)
The 28-day mortality of confirmed COVID-19 patients		
▪ Survivor	55 (57.9)	
▪ Non-survivor	40 (42.1)	
SAPS-3 **		37 (5-92)

***** *Data presented in mean ± standard deviation with normal data distribution*

*** Data presented in median (minimum-maximum) with abnormal data distribution.*

Bivariate analysis was performed on 95 subjects with confirmed COVID-19. Analysis of the SAPS 3 variables showed age, location of care before admission to the ICU, chronic heart failure, use of vasoactive drugs before ICU, reasons for admission in the form of focal neurological deficits and any other causes, acute infection during admission, GCS score, creatinine level, pulse rate, leucocyte level, platelet count, and oxygenation were significant correlates with 28-days mortality in the confirmed patients (Table 2).

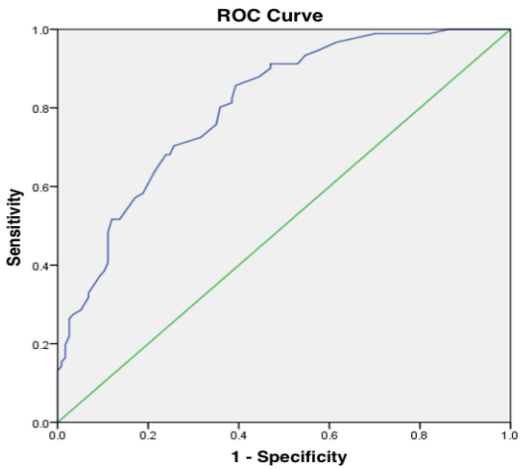

Figure 1: ROC curve, sensitivity, specificity score of SAPS 3in predicting 28-days mortality. AUC 0.805 (CI 95% 0.747−0.862; P > 0.001

We conducted a discrimination test and calibration between the SAPS 3 scores with 28-day mortality in ICU patients on COVID-19 confirmed cases. The value of the discrimination can be seen from the AUC value obtained from the ROC curve. The wider AUC represented a strong ability to discriminate. The AUC value obtained from the ROC curve was 0.805 (Figure 1), that showed a good predictability of SAPS-3 scores for 28-days mortality in the ICU. The *goodness-of-fit* analysis using the Hosmer-Lemeshow method showed a good model match value (P = 0.395). This value indicated that the calibration result was not significantly different from the actual value. Therefore, it can be assumed that the SAPS 3 score was able to predict 28-days mortality for confirmed COVID-19 patients in ICU.

Furthermore, the cut-off point of the SAPS 3 score was determined with the best sensitivity and specificity to predict the incidence of 28-day mortality of COVID-19 patients in the ICU. The sensitivity and specificity graph showed the cut-off point at score 39 with 70.3% sensitivity and 74.4% specificity. After obtaining the cut-off point value of 39, then a comparative analysis was conducted on scores more than 39 and less than 39. The analysis showed a significant result with 6.87 times mortality in the group with a score of SAPS 3 ≥ 39 (Table 3).

4. Discussion

There are several types of mortality predictors to analyze the pathophysiology of a disease, one of which is SAPS 3. It assesses the patient's condition since the

Table 2: Bivariate analysis of SAPS 3 variable and 28-day mortality in COVID-19 confirmed patients

Variable	N (%) (n = 95)	Non-survivors (n = 40)	Survivors (n = 55)	P value
Age				**0.001 ****
<40	22 (23.1)	3 (13.6)	19 (86.3)	
40-60	44 (46.3)	20 (45.4)	24 (54.5)	
60-70	20 (21.0)	11 (55)	9 (45)	
70-75	3 (3.15)	0 (0)	3 (100)	
75-80	3 (3.15)	3 (100)	0 (0)	
> 80	3 (3.15)	3 (100)	0 (0)	
LoS before ICU admission				0.396 **
<14 days	88 (92.6)	36 (40.9)	52 (59)	
15-28 days	6 (6.31)	4 (66.6)	2 (33.3)	
> 28 days	1 (1.05)	0 (0)	1 (100)	
In-hospital location before ICU admission	3 (3.15)	1 (33.3)	2 (66.6)	**0.006 ****
Operating room	58 (61.0)	17 (29.3)	41 (70.6)	
Emergency room	18 (18.9)	14 (63.6)	4 (33.3)	
Another critical room	63 (66.3)	8 (66.6)	55 (57.8)	
Others (ward)				
Comorbidity				
Malignancy	6 (6.31)	2 (33.3)	4 (66,6)	1,000 **
CHF	14 (14.7)	10 (71.4)	4 (28.5)	**0.016 ***
Cirrhosis	3 (3.15)	2 (66.6)	1 (33.3)	0.571 **
Metastases	-	-	-	-
Use of major therapeutic options before ICU admission: Vasoactive Drugs	42 (44.2)	32 (76.1)	10 (23.8)	**0.000 ***
ICU admission				0.603 *
Unplanned	76 (80)	33 (43.4)	43 (56.5)	
Well planned	19 (20)	7 (36.8)	12 (63.1)	
Reasons for ICU admission				
CVS - Rhythm disturbance	5 (5.26)	0 (0)	5 (100)	0.071 *
CVS - Hypovolemic shock	6 (6.31)	2 (33.3)	4 (66.6)	1.000 **
CVS - Septic shock	12 (12.6)	8 (66.6)	4 (33.3)	0.065 *
CVS - Shock of another type	-	-	-	-
Hepatic - Liver failure	1 (1.05)	1 (100)	0 (0)	0.421 **
Digestive - Severe pancreatitis	1 (1.05)	1 (100)	0 (0)	0.421 **
Digestive - Acute abdomen	3 (3.15)	1 (33.3)	2 (66.6)	1.000 **
Digestive - other	4 (4.21)	1 (25)	3 (75)	0.636 **
Neurological-effects of the intracranial mass	-	-	-	-
Neurologic-D focal neurological deficit	4 (4.21)	4 (100)	0 (0)	**0.029 ****
Neurological-Seizures	-	-	-	-
Neurological-Coma, stupor, delirium	-	-	-	-
Others				**0.000 ****
Respiratory failure	79 (83.1)	39 (49.3)	40 (50.6)	
Trauma	1 (1.05)	0 (0)	1 (100)	
Emergency surgery	1 (1.05)	1 (100)	0 (0)	
Surgical status at ICU admission				0.695 **
Scheduled surgery	5 (5.26)	2 (40)	3 (60)	
Emergency surgery	5 (5.26)	1 (20)	4 (80)	
No surgery	85 (89.4)	37 (43.5)	48 (56.4)	0.511 **

** Data were analyzed with Chi-square test, **analyzed with Fisher exact test*

Table 2: Bivariate analysis of SAPS 3 variable and 28-day mortality in COVID-19 confirmed patients (contd.)

Variable	N (%) (n = 95)	Non-survivors (n = 40)	Survivors (n = 55)	P value
Acute infection at ICU admission				**0.000 ****
Nosocomial infection	5 (5.26)	3 (60)	2 (40)	
Respiratory infection	63 (66.3)	35 (55.5)	28 (44.4)	
No infection	27 (28.4)	2 (7,4)	25 (92.5)	
GCS score (lowest)				**0.012 ****
3-4	1 (1.05)	1 (100)	0 (0)	
5	-	-	-	
6	-	-	-	
7-12	14 (14.7)	10 (71.4)	4 (28.5)	
> 12	80 (84.2)	29 (36.2)	51 (63.7)	
Total bilirubin (highest)				0.236 **
< 2 mg / dL	89 (93.6)	36 (40.4)	53 (59.5)	
2-5.9 mg / dL	6 (6.31)	4 (66,6)	2 (33.3)	
≥ 6 mg / dL	-	-	-	
Body temperature				
≥ 35 °C	95 (100)	40 (42.1)	55 (57.8)	-
Creatinine (highest)				**0.008 ****
<1.2 mg / dL	65 (68.4)	21 (32.3)	44 (67.6)	
1.2 - 1.99 mg / dL	18 (18.9)	9 (50)	9 (50)	
> 2 - 3.49 mg / dL	6 (6.31)	5 (83.3)	1 (16.6)	
≥ 3.5 mg / dL	6 (6.31)	5 (83.3)	1 (16.6)	
Heart rate (highest)				**0,000 ***
< 120 beats/min	83 (87.3)	29 (34.9)	54 (65)	
120-159 beats/min	12 (12.6)	11 (91.6)	1 (8,3)	
≥ 160 beats/min	-	-	-	
Leukocytes (lowest)				**0.010 ***
< 15	72 (75.7)	25 (34.7)	47 (65.2)	
≥ 15	23 (24.2)	15 (65.2)	8 (34.7)	
pH (lowest)				0.421 **
≤ 7.25	1 (1.05)	1 (100)	0 (0)	
> 7.25	94 (98.9)	39 (41.4)	55 (58.5)	
Platelets (lowest)				**0.029 ****
< 20,000 / µL	1 (1.05)	1 (100)	0 (0)	
20,000 - < 50,000 / µL	2 (2.10)	2 (100)	0 (0)	
50,000 – 100,000 / µL	1 (1.05)	1 (100)	0 (0)	
≥ 100,000 / µL	91 (95.7)	36 (39.5)	55 (60.4)	
Systolic blood pressure (mmHg)				0.924 *
< 40	-	-	-	
40 -69	-	-	-	
70 -119	29 (30.5)	12 (41.3)	17 (58.6)	
≥ 120	66 (69.4)	28 (42.4)	38 (57.5)	
Oxygenation				**0.001 ****
P / F < 100 with MV	13 (13.6)	9 (69.2)	4 (30.7)	
P / F > 100 with MV	17 (17.8)	10 (58.8)	7 (41.1)	
PaO_2 < 60 without MV	6 (6.31)	5 (83.3)	1 (16.6)	
PaO_2 > 60 without MV	59 (62.1)	16 (27.1)	43 (72.8)	

** Data were analyzed with Chi-square test, **analyzed with Fisher exact test; MV* = mechanical ventilation

Table 3: Comparison of SAPS 3 based on cut-off points and mortality

SAPS-3	Mortality		P value	Odds ratio
	Died	Alive		
≥ 39	64 (68.1)	30 (31.9)	0,000 *	6.87
< 39	27 (23.7)	87 (76.3)		

Data was analyzed using the chi-square test

first admission to the hospital and evaluates the data obtained from the first hour of the patient's admission to the ICU.[5–7] There are 3 types of assessment in SAPS 3; assessment of chronic health status and previous therapy, conditions related to ICU admission, and physiological data when entering the ICU. According to a study conducted by Moreno et al., the assessment of a patient's chronic health status is very important in assessing the patient's prognosis.[7] An increase in the total score of SAPS 3 will affect patient outcomes.[3,8] A study conducted by Sakr et al. stated that patients with a total SAPS 3 score ≤ 40, have a 3% mortality risk, the total score 40-60 increases the mortality risk to 10%, and a total score of > 80 increases the mortality risk to 70%.[4] Another study conducted by Joao et al. in 2010 showed patients with a SAPS 3 score ≤ 57 had a higher survival rate than those with a score > 57, who had a 73.5% mortality rate.[9]

A study conducted by Aaron Mark et al. in 2014 in one hospital in the Philippines using SAPS 3 showed a good precision in predicting mortality in the ICU.[6] The use of SAPS 3 scoring system as a predictor of mortality for COVID-19 cases can be used prioritize the patients to be admitted to ICU.[10,11]

The use of severity of illness scores have been applied in ICU for assessment of mortality and as a foundation to compare between interventions. APACHE and SAPS 3 scores are the two most used scores. Recently, amidst the COVID-19 pandemic, both of the scores were used to evaluate patients with COVID-19 admitted to the ICU. Prior studies had conflicting findings using the two scores for COVID-19 patients, two studies underestimated the mortality and severity of the disease.[13] However, a study from Austria found that SAPS 3 had satisfactory performance in the prognostication of mortality in patients with COVID-19.[13] A recent study by Metniz et al. found the same result as the Austrian study and supported the idea.[14] Nevertheless, a similar study conducted in Brazil had contradicting results and found that SAPS 3 failed to predict hospital mortality in ICU patients with COVID-19.[13] Thus, a study to evaluate prognostication of SAPS 3 was warranted in Indonesia.

The choice of SAPS 3 over APACHE II is based on that SAPS 3 has a more complete assessment of the patient's lung condition (PaO2/FiO2 ratio) compared to APACHE II. Patients with COVID-19 primarily have oxygenation problems furthermore the presence of evaluating the PaO2/FiO2 ratio helps to discriminate SAPS 3 in predicting mortality of COVID-19 patients in the ICU. In addition, the outcome of COVID-19 is highly associated with patients' comorbidities. SAPS 3 could assess the types of comorbidities as a reason to be admitted to the ICU. With this reasoning, we chose SAPS III instead of APACHE II for this study.

The study recruited 208 patients with probable and confirmed COVID-19 infection admitted in the ICU. The male patient percentage was 69.2% (144 patients) and the overall mean age was 50.6 years. These findings were similar to a study in France about COVID -9 patients in ICU that the majority of subjects were male (74%) and the average age was 60 years.[15] Research shows women are less susceptible to COVID-19 infection than men because of the X chromosome and sex hormones which played an important role in innate and adaptive immunity. In addition, men also tend to have a poor lifestyle such as smoking and other unhealthy lifestyles.[16,17] In our study, the median ICU hospitalization was 9 days. The results obtained in this study were similar to previous research which stated that the length of stay in the ICU in COVID-19 patients ranges from 6 to 12 days.[18] The mortality rate in our study subjects was high (43.8%), which indicated the need for a prognostic instrument to assess the severity of the condition to be treated more intensive in ICU to reduce the mortality.

Our study showed that older age had higher mortality than the younger age, with significant results at the age of 75-80 years and > 80 years, with 25-30 times higher mortality rates compared to age < 40 years. A previous study stated the CFR increased in the elderly with 10.9% percentage at the age 70-79 and 14.8% on those at the age of > 80 years. Other studies in Italy showed similar results that mortality risk increased significantly in populations at the age of > 70 years. Higher mortality in the older population was caused by the decrease of immunological properties resulting in increased susceptibility to infection. Other factors associated with older age were a higher incidence of comorbidity in the elderly that aggravated the symptoms of COVID-19 infection.[17]

Previous studies also concluded that reasons for ICU admission were one of the prognostics of patient mortality in the ICU that showed most of the patients

admitted to ICU were due to cardiovascular instability after surgical intervention. Our results were different from previous studies with the majority of subjects being admitted to ICU due to respiratory failure or septic shock. Most of our COVID-19 patients had respiratory failure due to severe ARDS or secondary infections causing septic shock and multi-organ failure and had higher mortality with 5 times of risk compared to other causes.[19,20]

We found the mortality risk was 4 times higher in COVID-19 patients with creatinine > 3.5 mg/dL, compared to if the creatinine was less than 1.2 mg/dL. The result was similar to previous studies. Increased serum creatinine in critically ill patients is associated with Acute Kidney Injury (AKI), which is one of the manifestations of multiorgan failure.[21,22] The initial phase of SARS-CoV-2 infection began with the host cell receptor binding and entering the cell using the ACE-2 protein that was expressed in various types of cells from multiple organs, thus those organs were considered vulnerable to SARS-CoV-2 infection, so that the non-respiratory symptoms may occur in patients with COVID-19. In addition, direct evidence of SARS-CoV-2 infection in the kidneys by performing an autopsy on one of the patients who died from COVID-19 found viral particles in the tubular epithelium of the kidney which was morphologically identical to SARS-CoV-2.[23]

Low platelets were also one of the mortality predictors in this study with more than 24 times increased mortality risk with platelets below 50,000 /µL to 20,000 /µL.[24] Previous studies have also shown that thrombocytopenia is associated with increased mortality, especially in patients with severe sepsis.[25]

Previous use of vasoactive drugs showed significant results with COVID-19 patients' mortality in the ICU. The use of vasoactive drugs is associated with a hypotensive state caused by hemodynamic instability and shock. Hypovolemia, tissue hypoperfusion, and sepsis could contribute to the etiology of shock in COVID-19 patients. Prognostic factors for vasoactive use showed the hemodynamic instability of COVID-19 patients in the ICU. Risk factors for shock in COVID-19 infection consist of older age, comorbidities (diabetes and cardiovascular), low lymphocyte values, and high D-dimers. Secondary infection in COVID-19 could result in septic shock and consequently need vasoactive treatment.[26]

SAPS 3 discrimination test on COVID-19 patients' 28-day mortality in the ICU reached 80.5% with AUC and was statistically significant. This result showed that SAPS 3 was able to predict 80.5% of subjects who had poor prognosis (> 80%). The calibration of the SAPS 3 questionnaire was also conducted in this study with the Hosmer-Lemeshow '*goodness of fit'* test which showed a good model fit with P = 0.395. This result showed that the model used in the SAPS 3 questionnaire can predict the mortality of patients with COVID-19 in the ICU better than the mortality that occurs in study subjects. The results obtained in this study were also similar to a previous study by Caler et al. However, this study failed to obtain good results on the calibration test with P < 0.05. In that study, poor calibration occurred due to a lower mortality rate at that hospital compared to other hospitals, causing an overestimation of the SAPS 3 prediction. Another study conducted by Hernandez, et al., showed similar discrimination results in SAPS 3 mortality prediction with good calibration.[6,27]

In this study, the SAPS 3 cut-off point to predict mortality was at a score of 39 with 70.3% sensitivity and 74% specificity. Based on the cut-off point, it was found that subjects with a SAPS 3 score ≥ 39 had 6.8 times higher risk of mortality with good sensitivity and specificity. A previous study conducted on non-COVID-19 elderly showed a SAPS 3 cut-off point of 57 with 84% sensitivity and 66% specificity. The obtained cut-off score in that study was higher compared to our study, which could be due to lower mortality. Until now, no previous studies have demonstrated the sensitivity and specificity of SAPS 3 for the mortality of COVID-19 patients in the ICU.[27]

5. Limitations

This study had some limitations. First, it was a retrospective study; and in early period of pandemic, medical record systems were transitioned into a newer system and caused missed data that had to be excluded from the sampling. This study collected secondary data from the medical records that were prone to recall or misclassification bias and could not determine causality. Although this study showed SAPS 3 was valid in predicting the 28-day mortality of critical COVID-19 patients, the results cannot represent the general COVID-19 population at large. The strength and validity of SAPS 3 would increase if the study was conducted further on a larger sample with a prospective multicenter study. However, the data will be useful for clinical assessment considering the high demand for ICU during the future COVID-19 waves or similar pandemics.

6. Conclusion

We found SAPS 3 variables, which significantly correlated with 28-day mortality in COVID-19 patients, were age, intra-hospital location before ICU admission, use of vasoactive drugs before ICU admission,

reason(s) for ICU admissions such as focal neurological deficits, respiratory failure, high creatinine level, and low platelets. This means that SAPS 3 score system was satisfactory in predicting the 28-day mortality of COVID-19 patients in the ICU with good discrimination and calibration value, therefore it's an important predictor tool for early prognosis screening that will help reduce the strain for hospitals' ICU.

7. Data availability

The numerical data generated during this research is available with the authors.

8. Acknowledgement

We are highly thankful to the ICU nursing staff of both of the hospitals, and the record office staff, who helped in data acquisition.

9. Conflicting Interest

The authors declare no conflicts of interest to disclose.

10. Authors' contribution

RBS, DA: Concept, Design, Literature search, Data acquisition, Statistical analysis, Manuscript preparation

SKM: Design, Literature search, Data acquisition, Statistical analysis, Manuscript preparation

PP: Literature search, Data acquisition, Statistical analysis, Manuscript preparation

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