Prediction of Mortality Using the Sequential Organ Failure Assessment Score in Critically Ill COVID-19 Patients

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ABSTRACT

Objective: To determine the accuracy and reliability of the sequential organ failure assessment (SOFA) score in predicting the risk of mortality in ICU-admitted COVID-19 patients.

Study Design: Cross-sectional study.

Place and Duration of the Study: COVID Intensive Care Unit (ICU), The Aga Khan University Hospital, Karachi, from January to June 2022.

Methodology: A total of 62 patients with a positive RT-PCR for COVID-19, admitted into the intensive care unit (ICU), were included in this descriptive cross-sectional study. Written informed consent was obtained after explaining the risks and benefits of the study to the patients / next of kin. SOFA score at the time of admission and 48 hours after admission was calculated. The outcome variable, i.e., mortality, was assessed in association with the SOFA score.

Results: The study had a predominantly male population of 54.8% (n = 34). The SOFA score >7 at admission and 48 hours after admission was observed in 46.8% (n = 29) patients. Among 62 COVID-19 patients, the majority were found to have a severe nature of the disease, i.e., 69.4% (n = 43), followed by moderate / mild cases 30.6% (n = 19). Depending on the requirement of the patient, 74.2% (n = 46) were invasively ventilated while 77.4% (n = 48) were on non-invasive ventilation. Overall the mortality rate of the present study was 43.5% (n = 27). The scores both at the time of admission and 48 hours after admission for the survivors had a significant difference (p = 0.001) with the non-survivors.

Conclusion: The SOFA score on admission and 48 hours after had a significant positive association with the severity of COVID-19 infection and its risk of mortality.

Key Words: *COVID-19, Mortality prediction, SOFA score.*

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INTRODUCTION

The COVID-19 outbreak emerged in 2019 in Wuhan, China. Within the next five months, six million new cases had been identified across 215 countries, and it was declared a pandemic by the WHO.[1,2] Apart from the majorly asymptomatic patients, a small minority developed severe symptoms with a grave clinical prognosis. Severe COVID-19 disease is usually complicated by the development of acute respiratory illness and hypoxia, which requires hospitalisation.[3] Among these, around 5-10% required intensive care unit (ICU) care and mechanical ventilation.[4]

During the first wave of this pandemic, 90% of the ICU beds were occupied by patients with severe COVID-19, resulting in a major bed shortage for other critical patients.[5]

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Due to the lack of clear guidelines pertaining to ICU admission and limited outcome data, decisions regarding admission and coding primarily relied on factors such as age and existing health conditions.[5] The outcome prediction models, such as acute physiology and chronic health evaluation (APACHE),[6] mortality probability models (MPM) systems,[7] and simplified acute physiology score (SAPS)[8] have been used in regular clinical practices.

The sequential organ failure assessment (SOFA) score was initially constructed in 1996 as a research tool for the sequential assessment and quantification of organ dysfunction severity in patients admitted to the ICU with sepsis.[9] A higher score indicates a worse prognosis and a greater likelihood of mortality.[10] This score has been used by many studies for mortality prediction in various clinical settings.[11-14] However, there is a dispute among studies regarding its prognostic accuracy. It has been used for mortality prediction during the COVID-19 pandemic.[15,16]

Although the SOFA score is validated in critical care patients, its validity in COVID-19 patients is not established. This study aimed to evaluate the prediction of mortality using the SOFA score in the population suffering from severe COVID-19.

METHODOLOGY

This cross-sectional study was conducted from January to June 2022, at the Aga Khan University Hospital, Karachi, Pakistan, in the COVID ICU, after the approval of the Ethics Review Committee (ERC No: 2021-6923-20042). Written informed consent was obtained after explaining the risks and benefits of the study to the patients / next of kin.

The sample size of 62 was calculated based on a mortality rate of 35.4%, with a 10% margin of error and 90% confidence level.[17] A non-probability consecutive sampling technique was employed. Patients older than 18 years, with a confirmed diagnosis of COVID-19 by polymerase chain reaction (PCR), and who were admitted to the ICU were included. The study did not include patients who died within the first 48 hours of admission or had an ICU length of stay of less than 48 hours. Patients with pre-existing multi-organ failure and pregnant females were also excluded from the study. Patients recruited in the study were followed from ICU admission till 48 hours. Demographic, laboratory, and clinical data collection was done with the help of a daily flow sheet. SOFA score calculation was done on admission and 48 hours after the admission. Values for each parameter at 0 and 48 hours were used for score calculation. All the findings of variables included in the study, such as age, gender, height, weight, body mass index (BMI), comorbidities, and invasive or non-invasive ventilation use, were noted down in the predesigned proforma.

RStudio (version 4.1.2; Boston, USA) was used for data analysis. Categorical variables, such as age, gender, BMI, and hypertension (HTN), were reported in frequency and proportion. Stratification of mortality was done for gender, BMI, the severity of COVID-19, comorbidity, use of invasive and non-invasive ventilation, and SOFA score at admission and 48 hours after admission. Post-stratification, the analytical tests, i.e., Chi-square and Fisher's exact tests, were employed to determine if there was an association between the study variables, such as age, comorbidities, and BMI with the severity of COVID-19 and resultant mortality. Univariate and multivariable binary logistic regression models were performed to identify potential factors correlated with mortality. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 62 patients were enrolled in this study. The patients' characteristics are shown in Table I. SOFA score >7 at admission and 48 hours after admission was observed in 46.8% (n = 29) of patients. Among 62 COVID-19 patients, the majority were found to have a severe nature of the disease, i.e., 69.4% (n = 43), followed by moderate / mild cases 30.6% (n = 19), according to the WHO COVID-19 severity classification. Depending on the requirement of the patient, 74.2% (n = 46) were invasively ventilated while 77.4% (n = 48) were on non-invasive ventilation. Overall, the mortality rate of the present study was 43.5% (n = 27). The association between predictors and mortality has been shown in Table II.

Table I: Patients' characteristics.

Variable	Total (n = 62)
Age (years)	
≤60	30 (48.4%)
>60	32 (51.6%)
Gender	
Female	28 (45.2%)
Male	34 (54.8%)
BMI (kg/m^2)	
<27.50	39 (62.9%)
≥27.50	23 (37.1%)
SOFA score at admission	
≤7	33 (53.2%)
>7	29 (46.8%)
SOFA score at 48 hours after admission	
≤7	33 (53.2%)
>7	29 (46.8%)
HTN	
No	16 (25.8%)
Yes	46 (74.2%)
DM	
No	24 (38.7%)
Yes	38 (61.3%)
Invasive mode of ventilation	
No	16 (25.8%)
Yes	46 (74.2%)
Non-invasive mode of ventilation	
No	14 (22.6%)
Yes	48 (77.4%)
Severity status of COVID-19	
Moderate / mild	19 (30.6%)
Severe	43 (69.4%)
Mortality	
No	35 (56.5%)
Yes	27 (43.5%)

Table II: Association between mortality and predictors.

Variable	Mortality status		p-value
	No (n = 35)	Yes (n = 27)	
Age (years)			
≤60	20 (57.1%)	10 (37.0%)	0.189*
>60	15 (42.9%)	17 (63.0%)	
Gender			
Female	14 (40.0%)	14 (51.9%)	0.501*
Male	21 (60.0%)	13 (48.1%)	
BMI (kg/m^2)			
<27.50	20 (57.1%)	19 (70.4%)	0.421*
≥27.50	15 (42.9%)	8 (29.6%)	
SOFA score at admission			
≤7	25 (71.4%)	8 (29.6%)	0.003*
>7	10 (28.6%)	19 (70.4%)	
SOFA score at 48 hours after admission			
≤7	31 (88.6%)	2 (7.4%)	<0.001**
>7	4 (11.4%)	25 (92.6%)	
HTN			
No	13 (37.1%)	3 (11.1%)	0.039*
Yes	22 (62.9%)	24 (88.9%)	
DM			
No	17 (48.6%)	7 (25.9%)	0.121*
Yes	18 (51.4%)	20 (74.1%)	
Invasive mode of ventilation			
No	16 (45.7%)	0 (0%)	<0.001**
Yes	19 (54.3%)	27 (100%)	
Non-invasive mode of ventilation			
No	10 (28.6%)	4 (14.8%)	0.235**
Yes	25 (71.4%)	23 (85.2%)	
Severity status of COVID-19			
Moderate / mild	19 (54.3%)	0 (0%)	<0.001**
Severe	16 (45.7%)	27 (100%)	

*p-value; *Chi-square or **Fisher's exact test.*

Table III: Univariate and multivariable logistic regression of age, gender, height, and weight.

Factors	crude OR (95% CI)	p-value	adj. OR (95% CI)	p-value
Age (years)				
≤60	Ref.		Ref.	
>60	2.27 (0.81 - 6.34)	0.119	0.62 (0.05 -7.97)	0.716
Gender				
Female	Ref.		Ref.	
Male	0.62 (0.23 - 1.71)	0.354	0.14 (0.01 - 2.10)	0.1536
BMI (kg/m^2)				
<27.50	Ref.		Ref.	
≥27.50	0.56 (0.19 - 1.63)	0.287	0.33 (0.03 - 4.15)	0.388
SOFA score at admission				
≤7	Ref.		Ref.	
>7	5.94 (1.97 - 17.92)	0.002	0.69 (0.08 - 5.68)	0.727
SOFA score at 48 hours after admission				
≤7	Ref.		Ref.	
>7	96.88 (16.38 - 572.88)	<0.001	123.63 (6.16 - 2483.22)	0.002
HTN				
No	Ref.		Ref.	
Yes	4.73 (1.19 - 18.83)	0.028	3.22 (0.07 - 156.13)	0.556
DM				
No	Ref.		Ref.	
Yes	2.70 (0.91 – 8.00)	0.073	0.224 (0.02 - 2.92)	0.253
Invasive mode of ventilation				
No	Ref.		Ref.	
Yes	164343019.70 (0 - Inf)	0.991	8108624.22 (0 - Inf)	0.996
Non-invasive mode of ventilation				
No	Ref.		Ref.	
Yes	2.30 (0.63 - 8.36)	0.206	4.29 (0.39 - 46.94)	0.233
Severity status of COVID-19				
Moderate / mild	Ref.		Ref.	
Severe	195157337.682(0 - Inf)	0.980	7572198.94 (0 - Inf)	0.996

BMI, DM, HTN, Invasive and non-invasive mode of ventilation, SOFA score at admission and 48 hours after admission.

This study showed a significant association of change in SOFA scores with mortality. The SOFA scores got worse over 48 hours in 33 patients. Out of which, 28 (84.8%) patients died (p <0.001). However, for patients whose SOFA scores got better or remained unchanged, no mortality was found.

Univariate and multivariate analyses revealed that the presence of hypertension significantly impacted the mortality status. However, the presence of diabetes, non-invasive ventilation, and age did not have a significant effect on the mortality status (Table III).

DISCUSSION

This observational study attempted to assess the predictive accuracy of the SOFA score in ICU-admitted COVID-19 patients. In all critical patients, a triage system is necessary to accurately estimate the likelihood of a fatal outcome and prioritise treatment accordingly. Extensive research has identified almost 60 predictors that can help physicians estimate the risk of a fatal outcome in patients who are severely ill due to COVID-19. Among these seven factors that have shown a strong correlation and consistency in predicting mortality risk are the SOFA score, age, C-reactive protein levels, body temperature, albumin levels, lactate levels, D-dimer levels, and the presence of comorbid conditions such as diabetes or heart failure.[18] However, no accurate system for triaging patients has been developed as of now.

The results of this survey showed that the SOFA score on admission and 48 hours after admission had a significant positive association with the severity of COVID-19 infection and its risk of mortality. Furthermore, this study also showed that the SOFA score decreased in 19 patients 48 hours after admission, and all these patients ultimately survived. In comparison, the SOFA score worsened in 33 patients after 48 hours and 28 (84.4%) patients were died. These statistics prove that the SOFA score is not only a good predictor of mortality, but the trend of rise or fall in the SOFA score can also serve as a key indicator of the ICU admitted patients' outcome. Similar findings have been reported by Martinez *et al*., who concluded that the increase in the SOFA score within the first 48 hours after admission is a significant predictor of mortality.[19] Similarly, in another study, the decrease in SOFA score was associated with a greater likelihood of survival, even after adjusting for age, gender, and comorbid conditions.[4] When the SOFA score is compared to other mortality predictor scores, such as the APACHE II, there is conflicting evidence regarding its predictive superiority. The results of a study conducted by Beigmohammadi *et al*. indicated that both scores demonstrated an association with increased mortality rates as the score values increased.[20] Notably, when a cut-off point of 13 was considered for APACHE II and 5 for the SOFA score, the daily SOFA score exhibited superior predictive performance. These findings highlight the relevance of using the SOFA score in prognosticating COVID-19 outcomes, underscoring its potential as a valuable tool for risk stratification and clinical decision-making. Against this, a comprehensive study by Zou *et al.* showed that when a cut-off value of 17 was used for the APACHE II and 3 for the SOFA, APACHE II better predicted hospital mortality.[21] This conflicting evidence emphasises that more studies with a transparent methodology and larger sample size need to be conducted to establish an accurate model for mortality prediction.

A study by Yang *et al.* reported that the median age of severely ill COVID-19 patients was 56 years, while the median age of patients with mild disease was 38 years.[22] The present study reaffirmed these findings, demonstrating that patients with severe COVID-19 were older compared to those with milder forms of the disease. Advanced age has consistently emerged as a significant factor in predicting both mortality and severity of COVID-19.[23] This can be attributed to the weakening of the immune system as age progresses and the greater likelihood of the presence of comorbid conditions. A weakened, dysregulated immune system cannot control the spread of infection and instead activates the cytokine storm syndrome in advanced disease stages.

Some studies have shown a positive association between the male gender and the severity of COVID-19.[23] However, this is only the case with a few studies. Studies with larger sample sizes depict an equal risk of the severity of COVID-19 across both genders.[20] The results of this study also showed that gender is not a valid predictor of the severity or mortality associated with the coronavirus disease.

The results of this study showed that patients with HTN had greater odds of expiring with COVID-19. This difference was significant, and HTN was a predictor of mortality in patients with severe coronavirus disease. Similarly, other comorbid conditions have unequivocally emerged as significant predictors of mortality in previous studies.[24,25] A previous history of diabetes mellitus, cardiovascular disease, cerebrovascular accident, and chronic obstructive pulmonary disease are associated with a proportionately increased risk of death in patients with COVID-19. An interesting theory explaining the high incidence of death among hypertensive patients with coronavirus infection has been proposed. The *SARS-COV-2* gains entry into the host cells *via* the angiotensin-converting enzyme 2 (ACE2) receptor. Hypertensive patients usually use ACE inhibitors (ACEI) or angiotensin receptor blockers (ARBs), which can cause upregulation of ACE2 receptors. This generates more entry points for the virus to enter the cells, resulting in a greater viral load and a more severe infection.[25] According to the results of this study, patients with diabetes had low odds of dying from COVID-19. However, this difference was insignificant, unlike other studies that state that diabetes can significantly predict the mortality risk in coronavirus-infected patients.[24] The smaller sample size of the survey can explain this difference.

This study had several limitations. Firstly, the data were gathered from patients in critical condition, which may have resulted in incomplete clinical information. Another key limitation was the calculation of the glasgow coma scale (GCS), as most patients in an ICU are sedated which hinders accurate GCS estimation. Many researchers have also highlighted this point as a major limitation of the SOFA score itself. Additionally, as the hospital serves as a tertiary care hospital and referral centre with multiple intensive care units, the high mortality rate observed in the study could be influenced by the specific patient population encountered during the study. Furthermore, given the ongoing uncertainties surrounding the characteristics of COVID-19, there is a pressing need for further studies to gain a deeper understanding of this disease.

CONCLUSION

The presence of comorbidities, particularly hypertension, increased age, and increased baseline and at 48 hours SOFA score following admission, significantly impacts the mortality status of admitted patients. Severity scoring systems, such as SOFA, have the potential to be used as a good tool for predicting mortality in COVID-19 patients. Furthermore, combining these scores with other clinical elements and imaging may help stratify the severity and risk of death from COVID-19.

ETHICAL APPROVAL:
The study was initiated after obtaining ethical approval from the Ethical Review Committee of the Aga Khan University, Karachi, Pakistan (ERC No: 2021-6923-20042).

PATIENTS' CONSENT:
A written informed consent was obtained from the patients.

COMPETING INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
MHK, BS: Acquisition, analysis and interpretation of the data, drafting, and revision of the manuscript.
MAA: Conception, design, and critical review of the manuscript for important intellectual content.
All authors approved the final version of the manuscript to be published.

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