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ORIGINAL ARTICLE

A single center retrospective observational study on the accuracy of the MuLBSTA score in predicting mortality among COVID-19 confirmed moderate to critical pneumonia cases

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ABSTRACT

Background: The coronavirus disease (COVID-19) is a global pandemic that caused millions of deaths worldwide. There is no standard risk stratification score for COVID-19 pneumonia. This study aims to determine the accuracy of the MuLBSTA score in predicting the risk of mortality in COVID-19 confirmed moderate to critical pneumonia cases.
Methodology: A total of 168 COVID-19-confirmed moderate to critical pneumonia patients admitted at Cardinal Santos Medical Center from January 1, 2021 to April 30, 2021 were included by chart review. The MuLBSTA score was determined for each patient using the following information: age, smoking history, co-morbidities, complete blood count, sputum culture, blood culture, chest x-ray and chest CT scan. All clinical outcomes were based on patient status by the end of the hospital stay (survival versus death). Thereafter, logistic regression was done using the MuLBSTA score and mortality to determine any correlation. In addition, modified regression was used to find any correlation with the MuLBSTA score and patient co-morbidities as predictors of mortality. Chi-square tests of independence were conducted to assess the specific cut-off values of the MuLBSTA score in predicting mortality.
Results: The MuLBSTA score is a significant predictor of mortality (73.08%) and survivability (66.67%). It was determined that the MuLBSTA score's accuracy in predicting mortality increases with diabetics [b = .26, p < .05]. In addition, the intervention of hemoperfusion can skew the predictive accuracy of the scoring [b = -.45, p<.01]. The study showed that a MuLBSTA score of 8 as a cut-off value to delineate high risk patients was more accurate in COVID-19 pneumonia patients compared to the previously established score cut-off of 12 in viral pneumonia [1].
Conclusion: The MuLBSTA score may be used for risk stratification in predicting mortality in COVID-19 pneumonia, especially among diabetic patients. A MuLBSTA score of 8 proves to be the more accurate cut-off in assessing risk of mortality in COVID-19. However, hemoperfusion makes the MulBSTA score inapplicable.

Introduction

The coronavirus disease (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV-2) was first reported in Wuhan, Hubei Province, China on December 1, 2019. Since its emergence, it has led to a global pandemic and has caused millions of deaths worldwide.

Scoring systems and risk factors for predicting mortality in COVID-19 patients are still being established. A lower lymphocyte count on admission was determined to be associated with severe COVID-19, the development of acute respiratory distress syndrome (ARDS), need for ICU care and increased mortality [2]. In addition, hypertension was noted to be associated with a composite poor outcome (severe COVID-19, ARDS, need for ICU, and mortality), especially for females, as cited in a meta-analysis by Pranata, *et al.* [3]. Given that there are many factors that can be correlated with mortality in COVID-19, a specific scoring system comprising the most significant risk factors is of great benefit. The MuLBSTA score is a predictive tool of mortality risk developed by Guo, *et al*. using the data of patients with confirmed viral pneumonia at RuiJin hospital, Shanghai from 2015 to 2019 [1]. The data was extracted from viral pneumonia patients infected with viruses – one of which was the coronavirus. Six significant factors were identified for mortality in viral pneumonia which comprise the MuLBSTA score namely: multilobar infiltrates, absolute lymphocyte count <0.8* 109/L, bacterial coinfection as determined by sputum or blood culture, smoking history, hypertension, and age > 60. This study showed a sensitivity of 0.776 and a specificity of 0.778 in predicting 90-day mortality in viral pneumonia and determined that a MuLBSTA score > 12 showed high risk for mortality.

Classic scoring systems such as CURB-65 score for pneumonia can be applied; however a standardized risk stratification specifically for COVID-19 infections has yet to be established. A study comparing CURB-65 with MuLBSTA concluded that the former is not recommended for assessment of patients with COVID-19. The proportion of MuLBSTA scores which are more than 12 points was much higher compared with the proportion of CURB-65 score more than 3 points in ICU care and deaths ($P < 0.05$), according to Xu, *et al.* in 2020 [4]. The study concluded that MuLBSTA yielded more high risk screens compared to CURB-65 when comparing ICU care and deaths. The MuLBSTA score was likewise evaluated by Iijima, *et al.* as a tool for monitoring COVID-19 disease progression, showing no disease progression noted if MuLBSTA score is less than 5 (a sensitivity of 100% and a specificity of 34.5%) [5]. Compared to PSI and CURB 65, the MuLBSTA score performed better in stratification for need for ICU admission [6]. MuLBSTA was likewise recommended as the primary choice for assessing risk of death in comparison to APACHE-II and CURB 65 [7]. This scoring system may prove to have a great potential in guiding health care professionals in management of COVID-19 pneumonia patients. The MuLBSTA score may be used as an objective basis for risk stratification and may guide further management.

1.1 Objectives of the study

The primary objective of the study is to validate the MuLBSTA score for mortality in COVID-19 moderate to critical pneumonia using patient information on admission. The specific objectives were to determine the predictive value of the MuLBSTA score in determining risk for mortality and to correlate the MuLBSTA score with comorbidities (i.e. DM) and hemoperfusion.

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Methodology

This study was a retrospective observational study approved by the Institutional Review Board and Ethics Committee of the Cardinal Santos Medical Center (CSMC). The study was conducted by chart review of patient data from COVID-19 moderate to critical pneumonia cases admitted in Cardinal Santos Medical Center from January 1, 2021 to April 30, 2021. The patient demographic data–age, smoking history, co-morbidities–and ancillary data: complete blood count, sputum cultures, blood cultures, chest x-ray and chest CT scan, were retrieved for data analysis. The clinical outcome was based on the patient status at the end of the hospital stay – survival vs death. An odds ratio of 9.74 was determined using an earlier study of Guo, *et al.* on the MuLBSTA score using a cut-off of 12. Using this odd's ratio and with a statistical power of 95 at 99% confidence interval–a minimum number of 153 patients was determined.

The study population consisted of adults (aged 19 and above) diagnosed with COVID-19 - confirmed moderate to critical pneumonia admitted within the first 10 days of illness. Only patients with COVID RT-PCR positive results during or prior to admission (within 10 days of onset of illness) were included. Patients with COVID reinfection, incomplete information precluding use of the MuLBSTA score, and patients initially managed in other institutions were excluded.

Study definition

- WHO COVID-19 Clinical Management Interim guidelines classification for:
  - Moderate pneumonia - clinical signs of pneumonia and requiring oxygen supplementation with nasal cannula or face mask but oxygen saturations 90% and above
  - Severe pneumonia - with oxygen saturations less than 90%, needing high flow oxygen
  - Critical pneumonia - respiratory distress and persistent hypoxemia needing intubation

Statistical Analysis

Statistical analysis was done using the Software Package for Social Sciences (SPSS) ver. 21 for Windows. Logistic regression was done at 95% confidence interval (p-value < 0.05) using the MuLBSTA score and mortality to determine its positive and negative predictive value. Moderated logistic regression was used to correlate the MuLBSTA score in predicting mortality in those with co-morbidities and those who underwent hemoperfusion. The chi-square test of independence was used to determine the predictive values of each MuLBSTA cut-off score. The Kaplan Meier survival analysis was done to further examine the significant cut-off scores for mortality in the MuLBSTA score.

Assessment of Biases

All patient records from the time period of January 1, 2021 to April 30, 2021 were included in this study to avoid selection bias and patient information was tabulated directly from patient records to limit recall bias and confounders were controlled by logistic regression analysis.

Ethical Considerations

This study was reviewed by the Institutional Review Board and Ethics Committee of CSMC. No conflict of interests from any financial, familial, or proprietary considerations of any sponsors were noted. The researchers provided a waiver of informed consent due to the retrospective nature of the study. Patient details were recorded under control numbers. Given the retrospective nature of the study (chart review) – no harm was done to the study population.

Results

A total of 275 patient records of COVID 19-confirmed moderate to critical pneumonia cases admitted at CSMC from January 1, 2021 to April 30, 2021 were retrospectively reviewed - of which 168 patients met the inclusion criteria. Upon admission, 77 patients (45.83%) were categorized as those with severe pneumonia, 73 patients (43.45%) were with moderate pneumonia, and 18 patients (10.71%) were critical. A majority of the patients were 60 years of age and above (55.95%), and females comprised a bigger percentage of the population (64.29%). A vast majority of the study population (133 of the 168; 79.17%) were non-smokers while the rest were subdivided into 33 previous smokers (19.64%) and only 2 active smokers (1.19%). The study population had the following comorbidities: hypertension (n= 110; 65.48%), diabetes (n=57; 33.93%), chronic kidney disease (n=11; 6.55%), and cancer (n=10; 5.95%). Multilobar pneumonia was more common among the patient population (152 of the 168 patients; 90.48%) while the rest of the subjects had less severe pulmonary infection on chest x-rays or chest CT scans. Absolute Lymphocyte Count (ALC) showed that only 67 of 168 patients (39.88%) had lymphopenia. Only 48 of 168 patients (28.57%) had culture proven bacterial coinfection while fungal infection was recorded in 19 patients (11.31%). About 118 of the 168 sample population (70.23%) had survived. Compared to the total sample population, the following are the proportions of mortalities by severity upon admission:

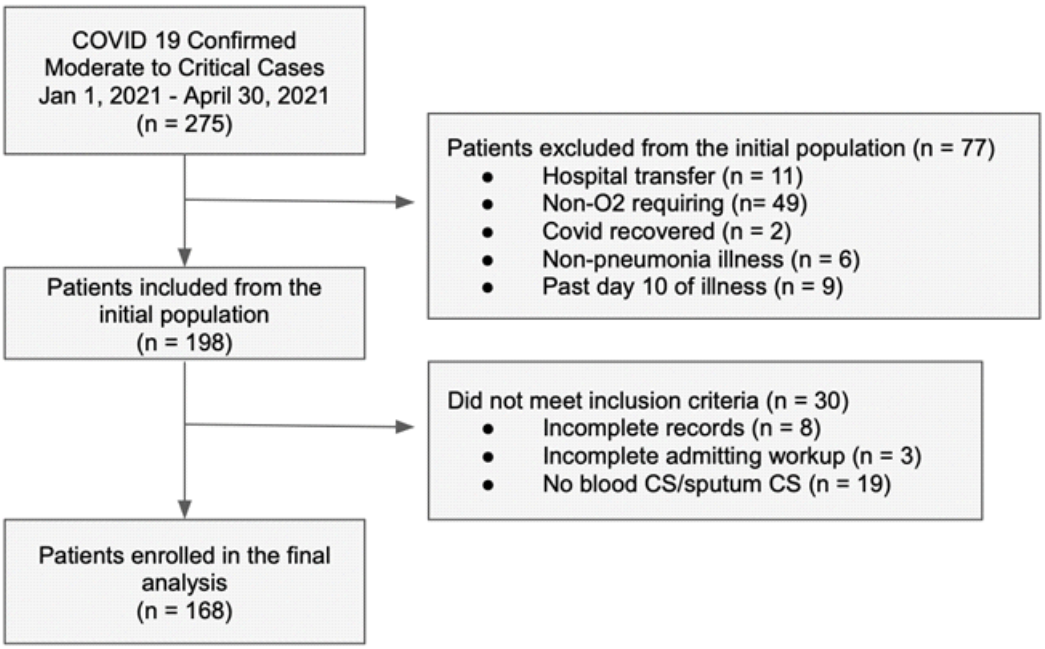

Figure 1. Diagram of Selection of Participants

7 of the 73 moderate cases (9.59%), 30 of the 77 severe cases (38.9%), and 13 of 18 of the critical cases (72.22%).

Logistic Regression

An initial binary logistic regression with MuLBSTA score as predictor and mortality as the outcome was conducted. The analysis showed that MuLBSTA was a positive and significant predictor of mortality [b(1) = .14, p <.01, r-squared = .05].

A moderated regression design with diabetes and hemoperfusion was done to further refine the regression model. Cancer and chronic kidney disease were not included in the moderated logistic regression because the chi-square dependent tests used were sensitive to their small sample sizes. The moderated binary logistic regression conducted showed that the MuLBSTA score, diabetes, hemoperfusion, and the interactions between MuLBSTA and diabetes, and MuLBSTA and hemoperfusion are significant predictors of mortality (LL (5) = 56.11, p < .001). The analysis showed that diabetes [b = -3.814, p<.05] was a negative predictor of mortality. However, the interaction between MuLBSTA and diabetes showed that it is a significant and positive predictor of mortality [b = .26, p < .05].

Hemoperfusion, on the other hand, was also a significant and positive predictor of mortality [b = 7.25, p<.001]. However, the interaction between MuLBSTA and hemoperfusion shows that hemoperfusion nullifies the predictive validity of MuLBSTA, showing higher rates of mortality regardless of MuLBSTA score [b = -.45, p<.01]. The analysis of the higher interaction between MuLBSTA, diabetes mellitus, and hemoperfusion shows that hemoperfusion negates both MuLBSTA and diabetes mellitus [p<.0001].

Chi-Square tests of independence

Chi-square tests of independence were conducted with each score to identify an ideal MuLBSTA cut-off score for mortality. The exact chi-square figure, p-value, relative risk, odds ratio, sensitivity, and specificity were also measured. Table 2 shows the summary of the results for each test.

Analysis of the cut-off scores showed that the more appropriate cut-off value ranged from MuLBSTA scores 8 through 11, of which MuLBSTA scores of 8 showed the best cut-off estimation to yield significant results (RR = 2.52, OR = 3.40, $\chi 2 = 7.93$, p < .01).

Kaplan-Meier Tests of Survivability

To further test the differences in survivability of the patients when using the different cut-off points, the researchers applied the Kaplan-Meier Tests of Survivability for MuLBSTA scores 8 through 11. Figure 2 shows the relationship of MuLBSTA with survivability showing the most consistent relationship with MuLBSTA scores of 8.

Discussion

MuLBSTA was shown to have a good predictive value for survivability (73.08%) and mortality (66.67%). Interestingly, this study showed that diabetes was a negative predictor of mortality. Diabetes incurs a two-fold risk for mortality and severity in a meta-analysis done by Kumar, *et al.* [8]. The negative predictive value of diabetes for mortality may be due to better health-seeking behavior of diabetic patients, who may seek consultation earlier in the course of disease. In addition, a meta-analysis showed that metformin reduces risk for mortality in diabetic patients [9]. This was also consistent with Kan, *et al.* in their systematic review on anti-diabetic agents and mortality in COVID-19. Metformin and sulfonylureas were associated with lower mortality risk among patients with COVID-19 [10]. These factors may be contributory to the negative predictive value of diabetes in this study.

The moderated regression results indicated that diabetes and hemoperfusion interacted with MULBSTA score – reflecting that diabetes increases the

Table 1. Logistic Regression Model for MuLBSTA as a Predictor of Mortality

		Observed		
		Expired	**Survived**	**Predictive Value**
Predicted	**Expired**	8	4	66.67%
	Survived	42	114	73.08%

Table 2. MuLBSTA Score and Overall Mortality Risk

MuLBSTA Score	n	Overall Death	Relative Risk	Odds-Ratio	Sensitivity	Specificity	$\chi 2$	p-value
0	3	0	N/A	N/A	1	0.0254	1.29	0.555
1	0	0	N/A	N/A	1	0.0254	1.29	0.555
2	1	0	N/A	N/A	1	0.0254	1.29	0.555
3	0	0	N/A	N/A	1	0.0338	1.74	0.319
4	5	2	N/A	N/A	1	0.0338	1.74	0.319
5	12	2	1.358	1.514	0.96	0.0593	0.26	1
6	3	0	1.643	1.936	0.92	0.1441	1.32	0.314
7	25	3	1.917	2.347	0.92	0.1695	2.3	0.154
8	**3**	**1**	**2.529**	**3.395**	**0.86**	**0.3559**	**7.93**	**.005****
9	**32**	**10**	**2.353**	**3.122**	**0.84**	**0.3729**	**7.45**	**.006****
10	**2**	**1**	**1.778**	**2.256**	**0.64**	**0.5593**	**5.58**	**.028***
11	**29**	**10**	**1.711**	**2.143**	**0.62**	**0.5678**	**4.96**	**.029***
12	2	1	1.571	1.946	0.42	0.7288	3.6	0.07
13	27	10	1.529	1.871	0.4	0.7372	3.13	0.098
14	0	0	1.5	1.857	0.2	0.8814	1.9	0.23
15	12	2	1.5	1.857	0.2	0.8814	1.9	0.23
16	0	0	2.476	5.429	0.16	0.9661	8.42	.007**
17	10	6	2.476	5.429	0.16	0.9661	8.42	.007**
18	0	0	3.458	N/A	0.04	0	4.77	0.087

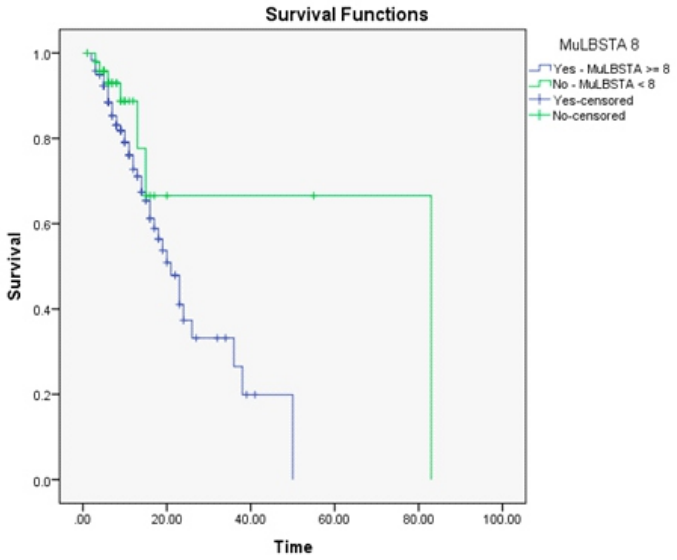

Figure 2. Kaplan-Meier Test of Survivability for MuLBSTA score 8

accuracy of the scoring and hemoperfusion can lessen its predictive value. Simply put, the MuLBSTA score becomes more accurate for patients with diabetes, hence it may be of greater benefit to use the MuLBSTA score in risk stratification of diabetic COVID-19 pneumonia patients. In contrast, for patients subjected to hemoperfusion, results show that regardless of the patient's MuLBSTA score mortality predictions were skewed compared to the non-hemoperfusion population. It was observed incidentally that there was a high rate of mortality for patients who underwent hemoperfusion even with MuLBSTA scores lower than the given cut-off value. However, the retrospective nature of this study limited the researchers' ability to investigate the details of the cases involved with hemoperfusion. From this study, what can be deduced is that the MuLBSTA score becomes inaccurate in predicting mortality among patients who underwent hemoperfusion.

While the cut-off scores of 8 through 11 show no significant difference in survivability, the optimal MuLBSTA score of 8 was determined to be the ideal cut-off for determining risk for mortality in COVID-19 pneumonia. This was supported by higher levels of relative risk (2.25), odds ratio (3.39), chi-square (7.93), and better Kaplan-Meier Survival measures of Logrank difference between groups. Mortality is 2.25 times more likely for COVID 19 patients that meet a MuLBSTA score of 8. The cut-off value of 8 was also determined in a similar study by George, *et al.* to be statistically significant in terms of mortality [11]. Thus we recommend that the threshold should be lowered from 12 so that patients may be managed more promptly as critical cases and with high risk of mortality.

Conclusions

The study showed that the MuLBSTA score is a positive and significant predictor of mortality [b(1) = .14, p <.01, r-squared = .05] with the potential to risk stratify patients upon admission. It was determined that a MuLBSTA cut-off score of 8 was shown to yield more significant results (RR = 2.52, OR = 3.40, $\chi 2$ = 7.93, p < .01) in predicting mortality in COVID-19. Further analysis showed that MuLBSTA was a stronger predictor of mortality in patients with diabetes [b = .26, p < .05] hence this study may advocate the application of the score in this particular patient population. Conversely, it was found that the risk of mortality was high in patients that underwent hemoperfusion regardless of their MuLBSTA score. Therefore the use of the MuLBSTA score might not be applicable to certain situations and should be applied to the appropriate patient populations.

Recommendation

The researchers recommend a multicenter study to represent the population better. In place of blood cultures and sputum cultures to document concomitant bacterial infection, future studies may try C-reactive protein (CRP) as a substitute as recommended by Iijima, *et al.* History with COVID-19 vaccination must be taken into account in future studies on MuLBSTA score and COVID-19 pneumonia. The exclusion of patients who had undergone hemoperfusion may produce more accurate results. More correlations may be made with a more extensive list of comorbidities included in data collection. A more consistent duration of observation may produce more uniform results (i.e. monitoring all patients until 90 days from onset of illness), although this will require outpatient follow-up of some cases.

References

1. Guo L, Wei D, Zhang X, Wu Y, Li Q, Zhou M, Qu J. (2020) Clinical Features Predicting Mortality Risk in Patients With Viral Pneumonia: The MuLBSTA Score. Front Microbiol. 2019 Dec 3;10:2752. doi:10.3389/fmicb.2019.02752. Erratum in: Front Microbiol. 11:1304. doi: 10.3389/fmicb.2020.01304. PMID: 31849894; PMCID: PMC6901688.
2. Huang I, Pranata R. (2020) Lymphopenia in severe coronavirus disease-2019 (COVID-19): systematic review and meta-analysis. J Intensive Care. 24(8):36. doi: 10.1186/s40560-020-00453-4. PMID: 32483488; PMCID: PMC7245646.
3. Pranata R, Lim MA, Huang I, Raharjo SB, Lukito AA. (2020) Hypertension is associated with increased mortality and severity of disease in COVID-19 pneumonia: A systematic review, meta-analysis and meta-regression. J Renin Angiotensin Aldosterone Syst. ;21(2):1470320320926899. doi: 10.1177/1470320320926899. PMID: 32408793; PMCID: PMC7231906.
4. Xu R, Hou K, Zhang K, Xu H, Zhang N, Fu H, Xie L, Sun R, Wen L, Liu H, Yang Z, Yang M, Guo Y. (2020) Performance of Two Risk-Stratification Models in Hospitalized Patients With Coronavirus Disease. Front Med (Lausanne). 14(7):518. doi: 10.3389/fmed.2020.00518. PMID: 32923449; PMCID: PMC7457082.
5. Iijima Y, Okamoto T, Shirai T, Mitsumura T, Sakakibara R, Honda T, Ishizuka M, Tateishi T, Tamaoka M, Aiboshi J, Otomo Y, Anzai T, Takahashi K, Miyazaki Y. (2021) MuLBSTA score is a useful tool for predicting COVID-19 disease behavior. J Infect Chemother. 27(2):284-290. doi: 10.1016/j.jiac.2020.10.013. Epub 2020 Oct 13. PMID: 33129694; PMCID: PMC7552979.
6. García Clemente MM, Herrero Huertas J, Fernández Fernández A, De La Escosura Muñoz C, Enríquez Rodríguez AI, *et al.* (2021) Assessment of risk scores in COVID-19. Int J Clin Pract. 75(12):e13705. doi: 10.1111/ijcp.13705. Epub 2020 Nov 21. PMID: 32931634.
7. Cheng P, Wu H, Yang J, Song X, Xu M, *et al.* (2021) Pneumonia scoring systems for severe COVID-19: which one is better. Virol J. 10;18(1):33. doi: 10.1186/s12985-021-01502-6. PMID: 33568204; PMCID: PMC7874994.
8. Kumar A, Arora A, Sharma P, Anikhindi SA, Bansal N, Singla V, Khare S, Srivastava A. (2020) Is diabetes mellitus associated with mortality and severity of COVID-19? A meta-analysis. Diabetes Metab Syndr. 14(4):535-545. doi: 10.1016/j.dsx.2020.04.044. Epub 2020 May 6. PMID: 32408118; PMCID: PMC7200339.
9. Lukito AA, Pranata R, Henrina J, Lim MA, Lawrensia S, Suastika K. (2020) The Effect of Metformin Consumption on Mortality in Hospitalized COVID-19 patients: a systematic review and meta-analysis. Diabetes Metab Syndr. 2020 Nov-Dec;14(6):2177-2183. doi: 10.1016/j.dsx.2020.11.006. Epub 2020 Nov 11. PMID: 33395778; PMCID: PMC7657016.
10. Kan C, Zhang Y, Han F, Xu Q, Ye T, Hou N, Sun X. (2021) Mortality Risk of Antidiabetic Agents for Type 2 Diabetes With COVID-19: A Systematic Review and Meta-Analysis. Front Endocrinol (Lausanne). 12:708494. doi: 10.3389/fendo.2021.708494. PMID: 34603199; PMCID: PMC8481667.
11. George R, Mehta AA, Paul T, Sathyapalan DT, Haridas N, Kunoor A, Ravindran GC. (2022) Validation of MuLBSTA score to derive modified MuLB score as mortality risk prediction in COVID-19 infection. PLOS Glob Public Health. 2(8):e0000511. doi: 10.1371/journal.pgph.0000511. PMID: 36962449; PMCID: PMC10021136.